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NEWS 4 OCT 07 Multiple databases enhanced for more flexible patent number searching
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NEWS 6 OCT 22 WPIDS, WPINDEX, and WPIX enhanced with Canadian PCT Applications
NEWS 7 OCT 24 CHEMLIST enhanced with intermediate list of pre-registered REACH substances
NEWS 8 NOV 21 CAS patent coverage to include exemplified prophetic substances identified in English-, French-, German-, and Japanese-language basic patents from 2004-present
NEWS 9 NOV 26 MARPAT enhanced with FSORT command
NEWS 10 NOV 26 MEDLINE year-end processing temporarily halts availability of new fully-indexed citations
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NEWS 15 DEC 17 Fifty-one pharmaceutical ingredients added to PS
NEWS 16 JAN 06 The retention policy for unread STNmail messages will change in 2009 for STN-Columbus and STN-Tokyo
NEWS 17 JAN 07 WPIDS, WPINDEX, and WPIX enhanced Japanese Patent Classification Data

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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NEWS LOGIN Welcome Banner and News Items

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of IPC 8

Enter NEWS followed by the item number or name to see news on that
specific topic.

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FILE 'HOME' ENTERED AT 18:02:17 ON 07 JAN 2009

=> FIL BIOSIS CAPLUS EMBASE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FILE 'BIOSIS' ENTERED AT 18:02:29 ON 07 JAN 2009
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=> s MAPX
L1          13 MAPX

=> s MAPC
L2         294 MAPC

=> s l2 and recombinant
L3           6 L2 AND RECOMBINANT

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4             3 DUP REM L3 (3 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L4   ANSWER 1 OF 3  BIOSIS  COPYRIGHT (c) 2009 The Thomson
Corporation  on STN
     DUPLICATE 1
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AN 2008:88063 BIOSIS
DN PREV200800088197
TI Stem cells and embryonic stem cells: Biological differences.
Original Title: Celulas madre y celulas troncoembrionarias: Diferencias
biologicas.
AU Riveros, Dolly Macias [Reprint Author]; Vazquez Chagoyan, Juan Carlos;
Morales, Rogelio Alonso; Juarez, Marco Cajero
CS Univ Autonoma Estado Mexico, Fac Med Vet and Zootecnia, Program Estudios
Avanzados Salud Anim, Km 15 5, Mexico City, DF, Mexico
marmac4@uaemex.mx; jcvc@uaemex.mx; ralonsom@servidor.unam.mx;
cajeromarco@hotmail.com
SO Veterinaria Mexico, (OCT-DEC 2007) Vol. 38, No. 4, pp. 477-501.
CODEN: VTERBU. ISSN: 0301-5092.
DT Article
LA Spanish
ED Entered STN: 23 Jan 2008
Last Updated on STN: 23 Jan 2008
AB The stem cells have been classified in three types according to their
natural nicheof origin, aptitude and differential function: totipotential,
pluripotential and multipotential; the first, called embryonic stem cells
(ES) originate from the morulae; the second, come from the inner cell mass
of the blastocyst (ICM); and the third, known as multipotent adult
progenitor cells (MAPC are found in some adult tissues. The
biological difference lies in their capabilities to produce cell lines,
the totipotentials have the faculty to originate a complete organism, the
pluripotential can generate all the cellular types and even the germinal
line and the multipotentials can derivate in specific lineages. The stem
cells are able to self-renew, and originate daughter-cells compromised
with certain development routes; they are characterized for their
indefinite division and are morphologically and functionally
differentiated. When the stem cells and some progenitor types are
extracted from their natural environment and are grown in vitro, in
suitable medium, can be transfected and remain in an undifferentiated
state without losing their potentiality; thus, when they are reintegrated
to blastocyst receptors they are able to go on with their development.

The study and compilation of information about these biological qualities of differential function, as well as their usefulness in homologous recombination and production of animal models that generate recombinant proteins, applicable for preventive-regenerating medicine and treatment of diseases, constitute the aim of this work.

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:493864 CAPLUS
DN 141:66248
TI Homologous recombination in multipotent adult progenitor cells
IN Verfaillie, Catherine; Lakshmipathy, Uma
PA Regents of the University of Minnesota, USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004050859	A2	20040617	WO 2003-US38811	20031125
WO 2004050859	A3	20040812		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003298016	A1	20040623	AU 2003-298016	20031125
US 20060228798	A1	20061012	US 2006-536716	20060530
PRAI US 2002-429631P	P	20021127		

WO 2003-US38811 W 20031125
AB The invention relates to methods of altering gene expression by homologous
recombination in a multipotent adult progenitor cell (MAPC). In particular, methods of producing a recombinant MAPC,
of correcting a genetic defect in a mammal, of providing a functional
and/or therapeutic protein to a mammal, and of transforming and differentiating a MAPC are provided. MAPCs containing an exogenous
DNA as well as recombinant MAPCs and their differentiated progeny are also provided. The examples disclose gene targeting and
genetic correction of a mutation in the FANCC protein, involved in Fanconi
anemia, in mouse MAPCs, followed by transplantation of the corrected cells into
FANCC-/- mouse and subsequent reversal of the FANCC deficiency.

L4 ANSWER 3 OF 3 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
DUPLICATE 2
AN 2005:65444 BIOSIS
DN PREV200500061976
TI Activated protein C preserves functional islet mass after intraportal
transplantation - A novel link between endothelial cell activation,
thrombosis, inflammation, and islet cell death.
AU Contreras, Juan L. [Reprint Author]; Eckstein, Christopher; Smyth, Cheryl
A.; Bilbao, Guadalupe; Vilatoba, Mario; Ringland, Sharman E.; Young,
Carlton; Thompson, J. Anthony; Fernandez, Jose A.; Griffin, John H.;
Eckhoff, Devin E.
CS 748 Lyons Harrison Res Bldg,701 19th St S, Birmingham, AL, 35294, USA
juan.contreras@ccc.uab.edu
SO Diabetes, (November 2004) Vol. 53, No. 11, pp. 2804-2814. print.
ISSN: 0012-1797 (ISSN print).
DT Article
LA English
ED Entered STN: 9 Feb 2005
Last Updated on STN: 9 Feb 2005
AB Clinical studies indicate that significant loss of functional islet mass
occurs in the peritransplant period. Islets are injured as a result of
detrimental effects of brain death, pancreas preservation, islet isolation, hypoxia, hyperglycemia, and immune-mediated events. In

addition, recent studies demonstrated that islets are injured as a result of their exposure to blood and of activation of intrahepatic endothelial and Kupffer cells, resulting in inflammation and thrombosis. Activated protein C (APC) is an anticoagulant enzyme that also exerts anti-inflammatory and antiapoptotic activities by acting directly on cells. Here, we report that exogenous administration of recombinant murine APC (mAPC) significantly reduced loss of functional islet mass after intraportal transplantation in diabetic mice. Animals given mAPC exhibited better glucose control, higher glucose disposal rates, and higher arginine-stimulated acute insulin release. These effects were associated with reduced plasma proinsulin, intrahepatic fibrin deposition, and islet apoptosis early after the transplant. In vitro and in vivo data demonstrated that mAPC treatment was associated with a significant reduction of proinflammatory cytokine release after exposure of hepatic endothelial cells to islets. mAPC treatment also prevented endothelial cell activation and dysfunction elicited by intrahepatic embolization of isolated islets inherent to pancreatic islet transplantation (PIT). This study demonstrates multiple remarkable beneficial effects of mAPC for PIT and suggests that A-PC therapy may enhance the therapeutic efficacy of PIT in diabetic patients.

=> s Furcht/au
L5 0 FURCHT/AU

=> s l1 and Furcht
L6 0 L1 AND FURCHT

=> s l1 and homlogous recombin?
L7 0 L1 AND HOMLOGOUS RECOMBIN?

=> s l1 and homologous recombin?
L8 0 L1 AND HOMOLOGOUS RECOMBIN?

=> d his

(FILE 'HOME' ENTERED AT 18:02:17 ON 07 JAN 2009)

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     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 18:02:29 ON 07 JAN 2009
L1            13 S MAPX
L2           294 S MAPC
L3             6 S L2 AND RECOMBINANT
L4             3 DUP REM L3 (3 DUPLICATES REMOVED)
L5             0 S FURCHT/AU
L6             0 S L1 AND FURCHT
L7             0 S L1 AND HOMLOGOUS RECOMBIN?
L8             0 S L1 AND HOMOLOGOUS RECOMBIN?

=> s l2 and furcht
L9             0 L2 AND FURCHT

=> s l2 and homologous recombin?
L10            3 L2 AND HOMOLOGOUS RECOMBIN?

=> dup rem l10
PROCESSING COMPLETED FOR L10
L11            2 DUP REM L10 (1 DUPLICATE REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L11  ANSWER 1 OF 2  BIOSIS  COPYRIGHT (c) 2009 The Thomson
Corporation  on STN
     DUPLICATE 1
AN   2008:88063  BIOSIS
DN   PREV200800088197
TI   Stem cells and embryonic stem cells: Biological differences.
     Original Title: Celulas madre y celulas troncoembrionarias:
Diferencias
     biologicas.
AU   Riveros, Dolly Macias [Reprint Author]; Vazquez Chagoyan, Juan
Carlos;
     Morales, Rogelio Alonso; Juarez, Marco Cajero
CS   Univ Autonoma Estado Mexico, Fac Med Vet and Zootecnia, Program
Estudios
     Avanzados Salud Anim, Km 15 5, Mexico City, DF, Mexico
     marmac4@uaemex.mx; jcvc@uaemex.mx; ralonsom@servidor.unam.mx;
     cajeromarco@hotmail.com
SO   Veterinaria Mexico, (OCT-DEC 2007) Vol. 38, No. 4, pp. 477-501.
     CODEN: VTERBU. ISSN: 0301-5092.
DT   Article
LA   Spanish
ED   Entered STN: 23 Jan 2008
     Last Updated on STN: 23 Jan 2008
AB   The stem cells have been classified in three types according to
their
     natural nicheof origin, aptitude and differential function:
totipotential,
     pluripotential and multipotential; the first, called embryonic
stem cells
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(ES) originate from the morulae; the second, come from the inner cell mass of the blastocyst (ICM); and the third, known as multipotent adult progenitor cells (MAPC are found in some adult tissues. The biological difference lies in their capabilities to produce cell lines, the totipotentials have the faculty to originate a complete organism, the pluripotential can generate all the cellular types and even the germinal line and the multipotentials can derivate in specific lineages. The stem cells are able to self-renew, and originate daughter-cells compromised with certain development routes; they are characterized for their indefinite division and are morphologically and functionally differentiated. When the stem cells and some progenitor types are extracted from their natural environment and are grown in vitro, in suitable medium, can be transfected and remain in an undifferentiated state without losing their potentiality; thus, when they are reintegrated to blastocyst receptors they are able to go on with their development.

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L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:493864 CAPLUS
DN 141:66248
TI Homologous recombination in multipotent adult progenitor cells
IN Verfaillie, Catherine; Lakshmipathy, Uma
PA Regents of the University of Minnesota, USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2004050859 A2 20040617 WO 2003-US38811
20031125
WO 2004050859 A3 20040812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
AU 2003298016 A1 20040623 AU 2003-298016
20031125
US 20060228798 A1 20061012 US 2006-536716
20060530
PRAI US 2002-429631P P 20021127
WO 2003-US38811 W 20031125
AB The invention relates to methods of altering gene expression by
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progenitor cell (MAPC). In particular, methods of producing a
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and of
transforming and differentiating a MAPC are provided. MAPCs
containing an exogenous DNA as well as recombinant MAPCs and
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differentiated progeny are also provided. The examples disclose
gene
targeting and genetic correction of a mutation in the FANCC
protein,
involved in Fanconi anemia, in mouse MAPCs, followed by
transplantation of
the corrected cells into FANCC-/- mouse and subsequent reversal
of the FANCC
deficiency.

=> s multipotent adult stem cell or multipotent adult progenitor cell
L12 170 MULTIPOTENT ADULT STEM CELL OR MULTIPOTENT ADULT
PROGENITOR CELL

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=> s l12 or l2
L13         387 L12 OR L2

=> s l13 and recombinant
L14           7 L13 AND RECOMBINANT

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15           4 DUP REM L14 (3 DUPLICATES REMOVED)

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 4 ANSWERS - CONTINUE? Y/(N):y

L15  ANSWER 1 OF 4  BIOSIS  COPYRIGHT (c) 2009 The Thomson
Corporation  on STN
     DUPLICATE 1
AN   2008:88063  BIOSIS
DN   PREV200800088197
TI   Stem cells and embryonic stem cells: Biological differences.
     Original Title: Celulas madre y celulas troncoembrionarias:
Diferencias
     biologicas.
AU   Riveros, Dolly Macias [Reprint Author]; Vazquez Chagoyan, Juan
Carlos;
     Morales, Rogelio Alonso; Juarez, Marco Cajero
CS   Univ Autonoma Estado Mexico, Fac Med Vet and Zootecnia, Program
Estudios
     Avanzados Salud Anim, Km 15 5, Mexico City, DF, Mexico
     marmac4@uaemex.mx; jcvc@uaemex.mx; ralonsom@servidor.unam.mx;
     cajeromarco@hotmail.com
SO   Veterinaria Mexico, (OCT-DEC 2007) Vol. 38, No. 4, pp. 477-501.
     CODEN: VTERBU. ISSN: 0301-5092.
DT   Article
LA   Spanish
ED   Entered STN: 23 Jan 2008
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     pluripotential and multipotential; the first, called embryonic
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     of the blastocyst (ICM); and the third, known as multipotent
adult
     progenitor cells (MAPC are found in some adult tissues.  The
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     the totipotentials have the faculty to originate a complete
organism, the
```

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L15 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:1006474 CAPLUS
DN 145:369871
TI Stably transformed bone marrow-derived cells and uses thereof for the treatment or diagnosis of heart or vascular diseases
IN Aikawa, Ryuichi; Losordo, Douglas W.
PA Caritas St. Elizabeth Medical Center Boston, Inc., USA
SO PCT Int. Appl., 92pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006102643	A2	20060928	WO 2006-US10981	20060324
	WO 2006102643	A3	20061116		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,

KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM
PRAI US 2005-665431P P 20050324
US 2005-673305P P 20050419
US 2005-735572P P 20051110
AB The invention provides compns. comprising genetically modified bone marrow
cells and related therapeutic and diagnostic methods. Transduced bone
marrow cells can be therapeutically administered to a subject, such as a
human patient to provide for the expression of an encoded protein in the
subject in need thereof. In particular embodiments, the invention
provides a method for expressing a therapeutic (e.g., IGF-1 or human
growth hormone) or reporter gene in a cardiac tissue or a blood vessel of
a host subject through hematopoietic stem cells stably transformed with a
recombinant adeno-associated viral vector for the treatment or
diagnosis of heart or vascular diseases.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:493864 CAPLUS
DN 141:66248
TI Homologous recombination in multipotent adult progenitor cells
IN Verfaillie, Catherine; Lakshmipathy, Uma
PA Regents of the University of Minnesota, USA
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DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO.
DATE

---------- ---- -------- ----------

PI WO 2004050859 A2 20040617 WO 2003-US38811
20031125
WO 2004050859 A3 20040812
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,
NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,
DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
AU 2003298016 A1 20040623 AU 2003-298016
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US 20060228798 A1 20061012 US 2006-536716
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PRAI US 2002-429631P P 20021127
WO 2003-US38811 W 20031125
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recombination in a multipotent adult
progenitor cell (MAPC). In particular,
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protein to a mammal, and of transforming and differentiating a
MAPC are provided. MAPCs containing an exogenous DNA as well as
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provided. The examples disclose gene targeting and genetic
correction of
a mutation in the FANCC protein, involved in Fanconi anemia, in
mouse
MAPCs, followed by transplantation of the corrected cells into
FANCC-/- mouse
and subsequent reversal of the FANCC deficiency.

L15 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2009 The Thomson
Corporation on STN
DUPLICATE 2

AN 2005:65444 BIOSIS
DN PREV200500061976
TI Activated protein C preserves functional islet mass after intraportal
transplantation - A novel link between endothelial cell activation,
thrombosis, inflammation, and islet cell death.
AU Contreras, Juan L. [Reprint Author]; Eckstein, Christopher; Smyth, Cheryl
A.; Bilbao, Guadalupe; Vilatoba, Mario; Ringland, Sharman E.; Young,
Carlton; Thompson, J. Anthony; Fernandez, Jose A.; Griffin, John H.;
Eckhoff, Devin E.
CS 748 Lyons Harrison Res Bldg,701 19th St S, Birmingham, AL, 35294, USA
juan.contreras@ccc.uab.edu
SO Diabetes, (November 2004) Vol. 53, No. 11, pp. 2804-2814. print.
ISSN: 0012-1797 (ISSN print).
DT Article
LA English
ED Entered STN: 9 Feb 2005
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AB Clinical studies indicate that significant loss of functional islet mass
occurs in the peritransplant period. Islets are injured as a result of
detrimental effects of brain death, pancreas preservation, islet
isolation, hypoxia, hyperglycemia, and immune-mediated events. In
addition, recent studies demonstrated that islets are injured as a result
of their exposure to blood and of activation of intrahepatic endothelial
and Kupffer cells, resulting in inflammation and thrombosis. Activated
protein C (APC) is an anticoagulant enzyme that also exerts
anti-inflammatory and antiapoptotic activities by acting directly on
cells. Here, we report that exogenous administration of
recombinant murine APC (mAPC) significantly reduced loss
of functional islet mass after intraportal transplantation in diabetic
mice. Animals given mAPC exhibited better glucose control,
higher glucose disposal rates, and higher arginine-stimulated acute
insulin release. These effects were associated with reduced plasma
proinsulin, intrahepatic fibrin deposition, and islet apoptosis early
after the transplant. In vitro and in vivo data demonstrated that

mAPC treatment was associated with a significant reduction of proinflammatory cytokine release after exposure of hepatic endothelial cells to islets. mAPC treatment also prevented endothelial cell activation and dysfunction elicited by intrahepatic embolization of isolated islets inherent to pancreatic islet transplantation (PIT). This study demonstrates multiple remarkable beneficial effects of mAPC for PIT and suggests that A-PC therapy may enhance the therapeutic efficacy of PIT in diabetic patients.

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=> d his

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     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 18:02:29 ON 07 JAN 2009
L1            13 S MAPX
L2           294 S MAPC
L3             6 S L2 AND RECOMBINANT
L4             3 DUP REM L3 (3 DUPLICATES REMOVED)
L5             0 S FURCHT/AU
L6             0 S L1 AND FURCHT
L7             0 S L1 AND HOMLOGOUS RECOMBIN?
L8             0 S L1 AND HOMOLOGOUS RECOMBIN?
L9             0 S L2 AND FURCHT
L10            3 S L2 AND HOMOLOGOUS RECOMBIN?
L11            2 DUP REM L10 (1 DUPLICATE REMOVED)
L12          170 S MULTIPOTENT ADULT STEM CELL OR MULTIPOTENT ADULT
PROGENITOR C
L13          387 S L12 OR L2
L14            7 S L13 AND RECOMBINANT
L15            4 DUP REM L14 (3 DUPLICATES REMOVED)

=> s l13 and homologous recombin?
L16            3 L13 AND HOMOLOGOUS RECOMBIN?

=> dup rem l16
PROCESSING COMPLETED FOR L16
L17            2 DUP REM L16 (1 DUPLICATE REMOVED)

=> s hematopoietic stem cell
L18        51155 HEMATOPOIETIC STEM CELL

=> s l18 and homologous recombin?
L19           78 L18 AND HOMOLOGOUS RECOMBIN?

=> dup rem l19
PROCESSING COMPLETED FOR L19
L20           64 DUP REM L19 (14 DUPLICATES REMOVED)
```

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=> s l20 and py<=2002
L21         24 L20 AND PY<=2002

=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 24 ANSWERS - CONTINUE? Y/(N):y

L21  ANSWER 1 OF 24  BIOSIS  COPYRIGHT (c) 2009 The Thomson
Corporation  on STN
AN   2003:356518  BIOSIS
DN   PREV200300356518
TI   Cooperating Mutations Are Necessary for the Development of AML
in Mll-ELL
     Knock-In Mice.
AU   Luo, Roger T. [Reprint Author]; Kebriaei, Partow [Reprint
Author];
     Kaberlein, Joseph J. [Reprint Author]; Thirman, Michael J.
[Reprint
     Author]
CS   Hematology/Oncology, University of Chicago, Chicago, IL, USA
SO   Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No.
     508. print.
     Meeting Info.: 44th Annual Meeting of the American Society of
Hematology.
     Philadelphia, PA, USA. December 06-10, 2002. American Society of
     Hematology.
     CODEN: BLOOAW. ISSN: 0006-4971.
DT   Conference; (Meeting)
     Conference; Abstract; (Meeting Abstract)
     Conference; (Meeting Poster)
LA   English
ED   Entered STN: 6 Aug 2003
     Last Updated on STN: 6 Aug 2003
AB   The (11;19)(q23;p13.1) translocation in acute leukemia results
in the
     generation of a chimeric MLL-ELL fusion protein.  To determine
the
     consequences of expression of MLL-ELL in hematopoietic cells, we
used
     homologous recombination in murine embryonic stem cells
     to generate an Mll-ELL knock-in allele.  Although Mll-ELL
chimeric and
     heterozygous mice express the Mll-ELL fusion gene, none develped
acute
     leukemia spontaneously.  Serial blood counts and smears from
chimeric and
     heterozygous mice were analyzed monthly for 2 years with no
apparent
     hematopoietic phenotype.  In contrast, we previously reported
that all
     mice transplanted with hematopoietic cells transduced with an
MLL-ELL
```

retrovirus developed AML with a latency of 4-6 months. To determine whether a cooperating mutation was necessary to induce leukemia, a cohort of 10 heterozygous mice was treated with a single sublethal dose of N-ethyl-N-nitrosourea (ENU) at 100 mg/kg. As controls, wildtype littermates were treated with the same dose of ENU, and a second cohort of heterozygous mice was observed without ENU treatment. After 11 months of observation, 7 of 10 Mll-ELL knock-in mice treated with ENU have died from AML. None of the mice from either control group has developed leukemia or another malignancy. The morphologic appearance and flow cytometric analyses of the Mll-ELL leukemia cells were consistent with a monocytic or myelomonocytic phenotype, similar to that observed in patients with the (11;19)(q23;p13.1) translocation and in mice transplanted with hematopoietic cells retrovirally transduced with MLL-ELL. MLL-ELL is the first MLL chimeric fusion protein that results in the development of AML in both transplantation and knock-in mouse models of leukemia. Taken together, these data suggest that in addition to MLL-ELL, a cooperating mutation is necessary to induce acute leukemia. The contrast between the 2 models in the requirement for ENU to induce leukemia may be due to differences in the expression of the MLL-ELL chimeric protein, with expression driven by the retroviral LTR in the transplant model and by the endogenous murine Mll promoter in the knock-in model. Alternatively, the lack of the requirement for ENU in the retroviral transduction and transplantation model suggests that insertional mutagenesis by retroviral integration may provide a cooperating mutation necessary for leukemogenesis.

L21 ANSWER 2 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2002:400475 BIOSIS
DN PREV200200400475
TI Genetic regulation of hematopoietic stem cell

telomere length in mice.
AU Manning, E.; True, J.; Henckaerts, E.; Snoeck, H.; Geiger, H.; de Haan,
G.; Lu, L.; Williams, R.; Van Zant, G.
SO Experimental Hematology (Charlottesville), (June, 2002) Vol. 30, No. 6 Supplement 1, pp. 112. print.
Meeting Info.: 31st Annual Meeting of the International Society for
Experimental Hematology. Montreal, Quebec, Canada. July 05-09, 2002.
CODEN: EXHMA6. ISSN: 0301-472X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 24 Jul 2002
Last Updated on STN: 24 Jul 2002

L21 ANSWER 3 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2002:241252 BIOSIS
DN PREV200200241252
TI Selectin-ligand pairs mediate the early phases of stem cell transplantation.
AU Fuller, Jennifer A. [Reprint author]; Kale, Sujata; Kelly, Robert J.;
Lowe, John B.; Long, Michael W.
CS Immunology Program, University of Michigan, Ann Arbor, MI, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 475a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Apr 2002
Last Updated on STN: 17 Apr 2002
AB Knowledge regarding the molecular events of hematopoietic stem cell (HSC) homing during bone marrow transplant (BMT) is limited. The process of stem cell transplantation is reminiscent
of that by which leukocytes trafficking into sites of inflammation in
which selectin/ligand pairs tether leukocytes to activated vascular
endothelium. We reasoned that for HSC to home to the bone marrow, they
must first roll on E- and P-selectins constitutively expressed on bone

marrow endothelial cells. Selectin-ligands are active only when modified post-translationally by fucosylated oligosaccharide moieties represented by the sialyl Lewisx (sLex) tetrasaccharide determinant and its structural variants. Synthesis of such sialylated, fucosylated glycans is controlled by the lineage-specific expression of one or more distinct alpha(1,3) fucosyltransferases (FucTs). Only two alpha(1,3) FucTs, termed FucT-IV and FucT-VII, are expressed in leukocytes and their progenitors, and thus, control leukocyte selectin-ligand activity via alpha(1,3) fucosylation.

To address the role of selectin-ligands in BMT, we used mice made null for fucosyltransferase-IV (FucT-IV), -VII (FucT-VII), or both (DKO) by homologous recombination that are congenic with their C57B1/6 recipients. We first performed homing assays in which bone marrow non-adherent, low density (NALD) cells from FucT-null mice were transplanted into irradiated wild type (WT) mice. Donor cells were PKH26-stained and injected into the retro orbital sinus. At 3 hours post-injection, bone marrow, spleen and peripheral blood were examined by flow cytometry for the presence of PKH26+ cells. These data demonstrate a significant reduction in the seeding efficiency of FucT-IV, FucT-VII and DKO mouse cells (>twofold; p=0.04) into WT marrow. In previous studies, we demonstrated a profound transplantation defect in the FucT-VII-null and FucT-DKO HSCs, with only 30 and 15% of the animals engrafting at limiting cell dilutions, respectively (Kale, et al., ASH abstracts 1999). In order to determine whether HSC: selectin interactions are physiologically relevant (i.e., are not related to irradiation-induced inflammation and selectin-upregulation), we constructed parabiotic animals in which a WT and FucT-VII animal are conjoined. These parabiotic animals showed complete anastomosis in their blood supplies within one week. After six

weeks of parabiosis, a genotypic analysis of HSC progeny (i.e., hematopoietic progenitor cells; HSP) indicates that a FucT-mediated hematopoietic defect exists within the FucT-VII-null animals' bone marrow. Genotyping of individual HSC-derived hematopoietic colonies showed that the distribution between WT and null HPC in the marrow of the parabiotic WT animal is approximately 50% null and 50% WT whereas, in the bone marrow of the FucT-VII-null animals, 100% of the colonies are of the FucT-VII-null genotype. In summary, under myeloablative conditions, FucT-null HSC show a marked decrease in homing capacity and a profound transplantation defect. In non-irradiated parabiotic animals, FucT-positive cells (from the WT side) cannot enter FucT-null marrow as null animals' endothelial cells fail to express selectin-ligands. In contrast, FucT-null cells (that express selectins but not selectin-ligands) can enter WT animals' marrow in which the endothelial cells constitutively express selectin-ligands. We conclude that interactions between the carbohydrate Lex/sLex/VIM2 structures and constitutively expressed selectins in bone marrow venules play an essential role in HSC homing and engraftment.

L21 ANSWER 4 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2002:241171 BIOSIS
DN PREV200200241171
TI Targeting of CD34+ cells within the bone marrow for inducible transgenic expression of cre recombinase.
AU Huettner, Claudia S. [Reprint author]; Radomska, Hanna S. [Reprint author]; Okuno, Yutaka [Reprint author]; Nagy, Andras; Tenen, Daniel G. [Reprint author]
CS Hematology/Oncology, Harvard Institutes of Medicine, Boston, MA, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 454a-455a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Apr 2002
Last Updated on STN: 17 Apr 2002
AB The human CD34 gene encodes a type I transmembrane glycoprotein, which is
expressed among other cells on early progenitor cells/stem cells in the
bone marrow. Expression of the CD34 antigen decreases as hematopoietic
stem cells differentiate and it is absent on all mature blood cells. We
isolated the human CD34 locus from a human PAC library and had
characterized and evaluated this genomic fragment for the expression of
human CD34 as a reporter gene in stable cell lines and subsequently in
several founder lines of transgenic mice. This fragment spanning 112 kb
of the 5-flanking region and 24 kb of the 3- flanking regions of the CD34
gene was found to be sufficient for the expression of the human CD34 gene
in the bone marrow and other tissues of transgenic mice. Moreover, the
mRNA expression pattern of the exogenous gene was found to be similar to
that of the endogenous murine CD34 gene in all tissues examined. FACS
analysis demonstrated that expression of CD34 decreases with maturation of
the cells. Three CD34 positive cell populations within the transgenic
bone marrow were identified: hCD34+/mCD34-, hCD34+/mCD34+ and
hCD34-/mCD34+. We have transplanted purified fractions of these cells
(described in Okuno et al.) and found that bone marrow cells expressing
the human CD34 transgene contain hematopoietic stem cells with long-term
reconstitution activity, while they are not contained in the cell
population expressing the endogenous murine CD34 gene. In order to
determine if the elements enclosed within this PAC clone are sufficient
for driving the expression of heterologous genes, we used
homologous recombination in bacteria to modify the
construct by inserting the sequence of the transactivator protein tTA,
which is part of the tetracycline responsive expression system. The

plasmid was linearized and the construct was injected into fertilized
murine oocytes. Animals transgenic for this construct termed CD34tTA were
cross bred with mice that carry the gene for are recombinase under control
of a tetracycline responsive element (TRE-cre). Expression of
transresponder cre gene in this transgenic system will be suppressed in
the presence of tetracycline, while in the absence of the antibiotic
expression will be induced. Analysis of double transgenic animals by
Northern Blot demonstrated cre expression in the heart, lung and the lymph
nodes 5 days after withdrawal of tetracycline, consistent with expression
of CD34 mRNA in the transgenic mice. As the human CD34 transgene is
expressed in only a few percent of bone marrow cells, we were unable to
detect cre mRNA expression by northern Blot, but could easily do so by
quantitative real Time PCR analysis. The expression in the heart was
determined to be more than seven-fold higher than in the bone marrow. The
lowest expression was seen in the liver in concordance with our data
generated by analyzing mice transgenc for the native CD34 locus. The
results are of particular interest as they show that the 160 kb expression
construct allows the targeting of CD34 positive cells within the bone
marrow and controlled expression of heterologous transgenes. The
CD34tTA-TRE-cre mice will allow for specific knock out of genes in CD34+
cells thus helping to elucidate the role of specific genes in
hematopoietic stem cells. Moreover, controlled expression in CD34+ cells
is important for experiments addressing the expression of heterologous
genes in stem cells, which may ultimately find applications in gene
therapy.

L21 ANSWER 5 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2001:314046 BIOSIS
DN PREV200100314046
TI Targeted integration of a GFP reporter into the SCA-1 locus results in

high level expression in hematopoietic cells of transgenic mice.
AU Meek, Sally C. [Reprint author]; Graubert, Timothy A. [Reprint author]
CS Internal Medicine, Division of Oncology, Section of Stem Cell Biology,
Washington University School of Medicine, St. Louis, MO, USA
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 663a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology.
San Francisco, California, USA. December 01-05, 2000. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002
AB To develop a system for targeting expression of genes to the hematopoietic stem cell compartment, we
employed Sca-1 (Ly-6A/E), a well-characterized marker of murine
hematopoietic stem cells. We assembled a targeting vector consisting of
5.2 kb of Sca-1 genomic sequence isogenic to our embryonic stem (ES) cell
line (129/SvJ strain, Ly-6A.2 allele). An enhanced green fluorescent
protein (GFP) cDNA (Clontech Labs, Palo Alto, CA) was inserted immediately
following the Sca-1 Kozak sequence in exon II. We removed the Sca-1
initiation codon and left the remaining genomic sequences intact. A
LoxP-flanked PGK-Neo cassette was subcloned downstream of the GFP
reporter. As an initial test of this construct, we electroporated it into
EL-4 cells, a murine B cell line that constitutively expresses high levels
of Sca-1. A small fraction (0.5-1.5%) of transiently transfected cells
demonstrated detectable GFP expression. A wide range of GFP activity was
evident in stable clones, suggesting that our targeting construct is
capable of directing high level expression after random integration into
hematopoietic cells. We then electroporated this construct into RW4 ES
cells and identified three clones that had undergone homologous
recombination. One of these clones was transiently transfected
with a plasmid encoding the Cre recombinase. We derived twelve correctly

targeted clones which had undergone excision of the PGK-Neo cassette. At this time, data is available from analysis of five chimeric founders obtained by injection of C57BL/6 blastocysts with one of the PGK-Neo (+) clones. Flow cytometric analysis of peripheral blood using the Ly-9.1 congenic marker demonstrated ES cell-derived hematopoiesis in a large proportion of leukocytes (range 31.8-73.6%) in these chimeric mice. GFP+ cells are easily detectable in peripheral blood from each of the animals, indicating that the Sca-1 targeting strategy successfully marked hematopoietic cells. The frequency of GFP+ cells correlates well with the degree of 129/SvJ chimerism and is surprisingly high (range 58.8-68.2% of ES-derived hematopoietic cells). However, approximately half of the GFP+ cells in each animal are Sca-1 negative, suggesting either increased post-transcriptional stability of the GFP reporter relative to the endogenous Sca-1 allele, or that expression of the targeted allele is dysregulated (possibly due to the retained PGK-Neo cassette). Analysis of F1 heterozygous mice (+/-PGK-Neo) should allow us to evaluate whether this system provides a valid strategy for genetically targeting hematopoietic stem cells in vivo.

L21 ANSWER 6 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2000:396218 BIOSIS
DN PREV200000396218
TI Molecules controlling hematopoietic development in vertebrates.
AU Cortes, Fernando; Labastie, Marie-Claude [Reprint author]
CS Institut d'Embryologie Cellulaire et Moleculaire, Cnrs UPR 9064, 49 bis, Avenue de la Belle-Gabrielle, 94736, Nogent-sur-Marne Cedex, France
SO M-S (Medecine Sciences), (Feb., 2000) Vol. 16, No. 2, pp. 198-204. print.
ISSN: 0767-0974.
DT Article
General Review; (Literature Review)
LA French
ED Entered STN: 13 Sep 2000

Last Updated on STN: 8 Jan 2002
AB Hematopoiesis first emerges in the embryo in the extra-embryonic mesoderm
in the yolk sac, and generates primitive erythoblasts. Definitive
hematopoiesis then takes place in the fetal liver and bone marrow probably
after the seeding of stem cells migrating from the para-aortic region.
The analysis of the phenotype of mutant mice created by homologous
recombination in ES cells has led to the identification of
mastegenes controlling hematopoietic development. These encode two types
of molecules, growth factors and transcription factors. Each appears to
act at a very timely defined stage of stem cell development, either to
specify the transition from the mesoderm to the hematopoietic
differenciation, or the choice between the lymphoid or myeloid pathway, or
to trigger the proliferation of defined progenitors. A hierarchy in the
activity of these genes has been proposed based on results of knock-out
experiments: in the absence of some of these molecules, hematopoiesis
completely fails to occur, whereas the lack of others only compromises the
development of one pathway. The ongoing challenge is now to unravel the
downstream signalling pathways used by these growth and transcription
factors to influence hematopoietic stem cell decisions.

L21 ANSWER 7 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1999:394228 BIOSIS
DN PREV199900394228
TI Biology of marrow stromal cell lines derived from long-term bone marrow
cultures of Trp53-deficient mice.
AU Epperly, Michael W.; Bray, Jenifer A.; Carlos, Timothy M.; Prochownik,
Edward; Greenberger, Joel S. [Reprint author]
CS Departments of Radiation Oncology, Pediatrics and Medicine, University of
Pittsburgh Cancer Institute, 200 Lothrop Street, Pittsburgh, PA, 15213,
USA
SO Radiation Research, (July, 1999) Vol. 152, No. 1, pp. 29-40.

print.
CODEN: RAREAE. ISSN: 0033-7587.
DT Article
LA English
ED Entered STN: 28 Sep 1999
Last Updated on STN: 28 Sep 1999
AB To investigate the effect of Trp53 (formerly known as p53) on stromal
cells of the hematopoietic microenvironment, long-term bone marrow
cultures were established from mice in which the Trp53 gene had been
inactivated by homologous recombination (Trp53-/-) or
their wild-type littermates (Trp53+/+). Long-term bone marrow cultures
from Trp53-/- mice continued to produce nonadherent cells for 22 weeks,
while Trp53+/+ cultures ceased production after 15 weeks. There was a
significant increase in the number of nonadherent cells produced in
Trp53-/- long-term bone marrow cultures beginning at week 9 and continuing
to week 22 ($P < 0.02$). The Trp53-/- cultures also showed significantly
increased cobblestone island formation indicative of early
hematopoietic stem cell-containing colonies
beginning at week 10 ($P < 0.01$). Cobblestone islands persisted until
weeks 15 and 22 in Trp53+/+ and Trp53-/- cultures, respectively.
Co-cultivation experiments in which Trp53+/+Scal+lin- enriched
hematopoietic stem cells were plated on Trp53-/- stromal cells showed
increased cobblestone island formation compared to Trp53-/- Scal+lin-
cells plated on Trp53+/+ or Trp53-/- stromal cells. Radiation survival
curves for clonal bone marrow stromal cells revealed a similar D0 for the
Trp53+/+ and Trp53-/- cell lines (1.62 +- 0.16 and 1.49 +- 0.08 Gy,
respectively; $P = 0.408$), and similar n (8.60 +- 3.23 and 10.71 +- 0.78,
respectively) ($P = 0.491$). Cell cycle analysis demonstrated a G2/M-phase
arrest that occurred 6 h after irradiation for both Trp53+/+ and Trp53-/-
stromal cell lines. After 10 Gy irradiation, there was no significant
increase in the frequency of apoptosis detected in Trp53+/+ compared to
Trp53-/- marrow stromal cell lines. In the stromal cell lines, ICAM-1 was

constitutively expressed on Trp53+/+ but not Trp53-/- cells; however, a
24-h exposure to TNF-alpha induced detectable ICAM-1 on Trp53-/- cells and
increased expression on Trp53+/+ cells. To test the effect of Trp53 on
the radiation biology of hematopoietic progenitor cells, the 32D cl 3 cell
line was compared with a subclone in which expression of an E6 inserted
transgene accelerates ubiquitin-dependent degradation of Trp53, thus
preventing accumulation of Trp53 after genotoxic stress. The radiation
survival curves were similar with no significant difference in the D0 or
n, or in the percentage of cells undergoing apoptosis after 10 Gy
irradiation between the two cell lines. Cells of the 32D-E6 cell line
displayed a G2/M-phase arrest 6 h after 10 Gy, while cells of the parent
line exhibited both a G2/M-phase arrest and a G1-phase arrest at 24 and 48
h. The results suggest a complex mechanism of action of Trp53 on the
interactions between stromal and hematopoietic cells in long-term bone
marrow cultures.

L21 ANSWER 8 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1997:448965 BIOSIS
DN PREV199799748168
TI Murine embryonic stem cells without pig-a gene activity are competent for
hematopoiesis with the PNH phenotype but not for clonal expansion.
AU Rosti, Vittorio; Tremml, Gabi; Soares, Vera; Pandolfi, Pier Paolo;
Luzzatto, Lucio [Reprint author]; Bessler, Monica
CS Dep. Human Genetics, Memorial Sloan Kettering Cancer Cent., 1275 York
Ave., New York, NY 10021, USA
SO Journal of Clinical Investigation, (1997) Vol. 100, No. 5, pp. 1028-1036.
CODEN: JCINAO. ISSN: 0021-9738.
DT Article
LA English
ED Entered STN: 27 Oct 1997
Last Updated on STN: 27 Oct 1997
AB Paroxysmal nocturnal hemoglobinuria (PNH) develops in patients who have

had a somatic mutation in the X-linked PIG-A gene in a hematopoietic stem cell; as a result, a proportion of blood cells are deficient in all glycosyl phosphatidylinositol (GPI)-anchored proteins. Although the PIG-A mutation explains the phenotype of PNH cells, the mechanism enabling the PNH stem cell to expand is not clear. To examine this growth behavior, and to investigate the role of GPI-linked proteins in hematopoietic differentiation, we have inactivated the pig-a gene by homologous recombination in mouse embryonic stem (ES) cells. In mouse chimeras, pig-a- ES cells were able to contribute to hematopoiesis and to differentiate into mature red cells, granulocytes, and lymphocytes with the PNH phenotype. The proportion of PNH red cells was substantial in the fetus, but decreased rapidly after birth. Likewise, PNH granulocytes could only be demonstrated in the young mouse. In contrast, the percentage of lymphocytes deficient in GPI-linked proteins was more stable. In vitro, pig-a- ES cells were able to form pig-a-embryoid bodies and to undergo hematopoietic (erythroid and myeloid) differentiation. The number and the percentage of pig-a-embryoid bodies with hematopoietic differentiation, however, were significantly lower when compared with wild-type embryoid bodies. Our findings demonstrate that murine ES cells with a nonfunctional pig-a gene are competent for hematopoiesis, and give rise to blood cells with the PNH phenotype. pig-a inactivation on its own, however, does not confer a proliferative advantage to the hematopoietic stem cell. This provides direct evidence for the notion that some additional factor(s) are needed for the expansion of the mutant clone in patients with PNH.

L21 ANSWER 9 OF 24 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 1996:432428 BIOSIS
DN PREV199699146034
TI Current experimental strategies for investigating human hematopoietic stem cell biology.
AU Ratajczak, Mariusz Z.; Gewirtz, Alan M.
CS Dep. Pathol., 515 Stellar-Chance Labs., 422 Curie Blvd., Univ. Pennsylvania Sch. Med., Philadelphia, PA 19104, USA
SO Folia Histochemica et Cytobiologica, (1996) Vol. 34, No. 2, pp.

59-67.
CODEN: FHCYEM. ISSN: 0239-8508.
DT Article
LA English
ED Entered STN: 26 Sep 1996
Last Updated on STN: 26 Sep 1996
AB The currently available different experimental strategies for investigating the biology of the human hematopoietic stem cells are reviewed in this paper. There are discussed: (1) different approaches to isolate human hematopoietic stem cells, (2) available molecular techniques for investigating gene expression in isolated cells, and (3) functional tests evaluating their proliferative potential in in vitro cultures and in vivo in animal models. Important information regarding stem cell biology can be also gained from animal model involving: (1) overexpression of particular genes in transgenic mice or, (2) gene "knock-out" techniques using homologous recombination. The regulation of proliferation and differentiation of human hematopoietic stem cells can be also discerned after downregulation of expression of genes of interest in the early hematopoietic cells using antisense strategy.

L21 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:37226 CAPLUS
DN 142:174056
TI Erythropoietic porphyrias: Animal models and prospects for cellular and gene therapy in human
AU Ged, Cecile; Moreau-Gaudry, Francois; de Verneuil, Hubert
CS Laboratoire de Pathologie Moleculaire et Therapie Genique, Universite Victor Segalen-Bordeaux II, Bordeaux, 33076, Fr.
SO Recent Research Developments in Human Genetics (2002), 1(Pt. 1), 253-271
CODEN: RRDHC6
PB Research Signpost
DT Journal; General Review
LA English
AB A review. Recent progress in mol. technol. has resulted in precise knowledge of the genes involved in the heme biosynthetic pathway as well as rapid development of innovative tools including animal models and gene

transfer strategies aimed at a better understanding of pathogenesis and
treatment of porphyrias. Animal models of erythropoietic porphyrias occur
naturally, are obtained by chemical mutagenesis, or created by
homologous recombination in transgenic mice. Successful
gene transfer expts. performed both in vitro, in hematopoietic progenitor
cells, and in vivo demonstrate the feasibility of somatic gene therapy in
erythropoietic porphyrias. Sufficient gene transfer rate, and convenient
metabolic correction in disease cells, as well. As phenotypic reversion
when a mouse model was available, have been documented in protoporphyria
(ferrochelatase deficiency) and congenital erythropoietic porphyria
(uroporphyrinogen III synthase deficiency). This confirms that
erythropoietic porphyrias are good candidates for the treatment of
hematopoietic stem cells by gene therapy.
RE.CNT 129 THERE ARE 129 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1994:601809 CAPLUS
DN 121:201809
OREF 121:36667a,36670a
TI The hematopoietic cell-specific gene D4 and it use in the study of
hematopoiesis
IN Lim, Bing; Lelias, Jean-Michel; Adra, Chaker N.; Ko, Jone L.
PA Cytomed, Inc., USA; Beth Israel Hospital Association
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9413802	A1	19940623	WO 1993-US12074	19931210 <--
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9457486	A	19940704	AU 1994-57486	19931210 <--
US 5767073	A	19980616	US 1994-252073	19940601 <--

US 5585478 A 19961217 US 1994-292945
19940818 <--
PRAI US 1992-990337 A 19921210
WO 1993-US12074 W 19931210
AB A cDNA clone, denoted D4, of human or mouse that is
preferentially
expressed in hematopoietic cells is cloned and expressed for use
in the
study of the function of the protein. The human cDNA clone has
been
expressed in bacteria and the predicted 24 Kd protein purified
and cDNA
was used to obtain several full length mouse genomic clones.
Sequence
comparisons indicate that D4 is similar to the bovine rhoGDI
protein and
so may function as a GDP-dissociation inhibitor of at least
several small
GTP-binding proteins (CDC42 and rac). The D4 protein was used
to generate
a polyclonal antibody sp. for the protein. A clone has been
analyzed and
sequenced to use for the construction of a gene-targeting vector
to
produce animals deficient in D4 through disruption of the gene by
homologous recombination. These animals can then be
used as models for fundamental and applied research on the
GTP-binding
proteins. Hematopoietic cell-specific cDNAs were cloned using
subtractive
libraries from hematopoietic stem cell lines
as probes for a cDNA library from K562 cells. Patterns of
transcription
of the gene in differentiating human cell lines in culture and in
developing mouse were determined and the restriction of
expression to
hematopoietic cells demonstrated although it may not be relevant
to
erythropoiesis or embryonic hematopoiesis.

L21 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1993:139047 CAPLUS
DN 118:139047
OREF 118:23706h,23707a
TI Targeted gene modification for gene therapy of stem cells
AU Boggs, Sallie S.; Bahnson, Alfred B.
CS Sch. Med., Univ. Pittsburgh, Pittsburgh, PA, USA
SO Concise Rev. Clin. Exp. Hematol. (1992), 319-30. Editor(s):
Murphy, Martin J., Jr. Publisher: AlphaMed, Dayton, Ohio.
CODEN: 58NOAO
DT Conference; General Review
LA English

AB A review with 117 refs. Ideally, gene therapy would correct the specific gene defect without adding potentially harmful extraneous DNA sequences. Such correction can be obtained by homologous recombination (HR) between newly added DNA sequences and identical (homologous) sequences in the genomic target. Hematopoietic stem cells (HSC) are the necessary targets for gene therapy of hemoglobinopathies. Unfortunately, the low efficiency of HR and the fact that HSC are rare, noncycling cells that are difficult to expand in culture makes HR in HSC impractical. However, technol. developments in HSC purification, culture, and assay, increasing knowledge of factors affecting HR efficiency, and powerful new selection systems are increasing the likelihood of using HR in HSC. Meanwhile, the ability of adeno-associated virus (AAV) to target a specific chromosome site in nondividing cells makes AAV vectors attractive for gene therapy with HSC. Alternately, embryo stem (ES) cells with genes modified by HR might be made to differentiate to HSC. These advances are reviewed with particular emphasis on approaches to targeted gene modification of HSC and speculation on directions for future research.

L21 ANSWER 13 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN

AN 2002352842 EMBASE

TI Lack of neighborhood effects from a transcriptionally active phosphoglycerate kinase-neo cassette located between the murine β-major and β-minor globin genes.

AU Kaufman, Richard M.; Lu, Zhi Hong; Behl, Rajesh; Holt, Jo M.; Ackers, Gary K.; Ley, Timothy J. (correspondence)

CS Division of Oncology, Section of Stem Cell Biology, Washington Univ. School of Medicine, 660 South Euclid Ave, St Louis, MO 63110-1093, United States. timley@im.wusti.edu

SO Blood, (1 Jul 2001) Vol. 98, No. 1, pp. 65-73.
Refs: 42
ISSN: 0006-4971 CODEN: BLOOAW

CY United States

DT Journal; Article
FS 025 Hematology
LA English
SL English
ED Entered STN: 31 Oct 2002
Last Updated on STN: 31 Oct 2002
AB For the treatment of β-globin gene defects, a homologous recombination-mediated gene correction approach would provide advantages over random integration-based gene therapy strategies. However, "neighborhood effects" from retained selectable marker genes in the targeted locus are among the key issues that must be taken into consideration for any attempt to use this strategy for gene correction. An Ala-to-Ile mutation was created in the β6 position of the mouse β-major globin gene (β(61)) as a step toward the development of a murine model system that could serve as a platform for therapeutic gene correction studies. The marked β-major gene can be tracked at the level of DNA, RNA, and protein, allowing investigation of the impact of a retained phosphoglycerate kinase (PGK)-neo cassette located between the mutant β-major and β-minor globin genes on expression of these 2 neighboring genes. Although the PGK-neo cassette was expressed at high levels in adult erythroid cells, the abundance of the β(61) mRNA was indistinguishable from that of the wildtype counterpart in bone marrow cells. Similarly, the output from the β-minor globin gene was also normal. Therefore, in this specific location, the retained, transcriptionally active PGK-neo cassette does not disrupt the regulated expression of the adult β-globin genes. .COPYRGT. 2001 by The American Society of Hematology.

L21 ANSWER 14 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights reserved on STN
AN 2000433831 EMBASE
TI Gene correction in hematopoietic progenitor cells by homologous recombination.
AU Hatada, Seigo; Bentley, Stuart A.; Smithies, Oliver (correspondence)
CS Dept. of Pathol. and Lab. Medicine, Lineberger Compreh. Cancer Center,

University of North Carolina, Chapel Hill, NC 27599-7525, United States.
jhlynch@med.unc.edu
AU Kirby, Suzanne
CS Department of Medicine, Lineberger Compreh. Cancer Center, University of
North Carolina, Chapel Hill, NC 27599-7525, United States.
AU Nikkuni, Koji
CS First Dept. of Internal Medicine, School of Medicine, Niigata University,
1-757 Asahimachi Street, Niigata City, Niigata 951, Japan.
AU Smithies, Oliver (correspondence)
CS Department of Pathology, Laboratory Medicine, University of North
Carolina, Chapel Hill, NC 27599-7525, United States.
jhlynch@med.unc.edu
SO Proceedings of the National Academy of Sciences of the United States of
America, (5 Dec 2000) Vol. 97, No. 25, pp. 13807-13811.
Refs: 24
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 022 Human Genetics
025 Hematology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 29 Dec 2000
Last Updated on STN: 29 Dec 2000
AB Homologous recombination (gene targeting) has many
desirable features for gene therapy, because it can precisely correct
mutant genes and restore their normal expression, and random nonhomologous
integration of DNA is infrequent in cells in which homologous
recombination has occurred. There are, however, no reports of
attempts to use homologous recombination to correct
mutant genes in normal hematopoietic stem cells (HSCs), which are prime
cells for therapy of a variety of hematological and other conditions,
presumably because of their low abundance and uncertainty that
homologous recombination can occur at a usable frequency
in these cells. The experiments reported here encourage optimism in this
respect by demonstrating targeted correction of a defective hypoxanthine
phosphoribosyltransferase gene in hematopoietic progenitor cells that can
form colonies in methylcellulose culture. These clonogenic cells are in
the same lineage as HSCs but are more abundant and more mature and so less

pluripotent. Corrected colonies were identified by their survival in
selective medium after electroporation of correcting DNA into unfractionated mouse bone marrow cells and were confirmed by reverse
transcription-PCR and sequencing. The observed frequency (4.4 ± 3.3 x
10(-5) per treated clonogenic cell) is the same as in embryonic stem cells
(2.3 ± 0.4 x 10(-5)) with the same DNA and mutation. These data
suggest that gene targeting to correct mutant genes eventually will prove
feasible in HSCs capable of long-term bone marrow reconstitution.

L21 ANSWER 15 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
reserved on STN
AN 2000303186 EMBASE
TI Thrombasthenic mice generated by replacement of the integrin α(IIb)
gene: Demonstration that transcriptional activation of this megakaryocytic
locus precedes lineage commitment.
AU Tronik-Le Roux, D. (correspondence); Roullot, V.; Poujol, C.; Kortulewski,
T.; Nurden, P.; Marguerie, G.
CS Commissariat a l'Energie Atomique, Dept. de Radiobiol. et Radiopathol.,
CEA-Evry, 2 rue Gaston Cremieux, 91057 Evry Cedex, France. leroux@dsvidf.c
ea.fr
SO Blood, (15 Aug 2000) Vol. 96, No. 4, pp. 1399-1408.
Refs: 60
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; Article
FS 025 Hematology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 21 Sep 2000
Last Updated on STN: 21 Sep 2000
AB To analyze the transcriptional activity of the gene encoding the α
subunit of the platelet integrin α(IIb)β(3) during the hematopoietic differentiation, mice were produced in which the herpes
virus thymidine kinase (tk) was introduced in this megakaryocytic specific
locus using homologous recombination technology. This provided a convenient manner in which to induce the eradication of

particular hematopoietic cells expressing the targeted gene. Results of
progenitor cell cultures and long-term bone marrow (BM) assays showed that
the growth of a subset of stem cells was reduced in the presence of the
antiherpetic drug ganci-clovir, demonstrating that the activation of the
toxic gene occurs before the commitment to the megakaryocytic lineage.
Furthermore the knock-in of the tk gene into the α(IIb) locus
resulted in the knock-out of the α(IIb) gene in homozygous mice.
Cultures of BM cells of these animals, combined with ultrastructural
analysis, established that the α(IIb) glycoprotein is dispensable
for lineage commitment and megakaryocytic maturation. Platelets collected
from α(IIb)-deficient mice failed to bind fibrinogen, to aggregate,
and to retract a fibrin clot. Moreover, platelet α-granules did not
contain fibrinogen. Consistent with these characteristics, the mice
displayed bleeding disorders similar to those in humans with Glanzmann
thrombasthenia. (C) 2000 by The American Society of Hematology.

AN 2000255733 EMBASE
TI Insertion of enhanced green fluorescent protein into the lysozyme gene
creates mice with green fluorescent granulocytes and macrophages.
AU Graf, Thomas (correspondence)
CS Albert Einstein College of Medicine, 1300 Morris Park Ave, Bronx, NY
10461, United States. graf@aecom.yu.edu
AU Faust, Nicole; Varas, Florencio; Kelly, Louise M.; Heck, Susanne
SO Blood, (15 Jul 2000) Vol. 96, No. 2, pp. 719-726.
Refs: 20
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; Article
FS 025 Hematology
LA English
SL English
ED Entered STN: 10 Aug 2000
Last Updated on STN: 10 Aug 2000
AB Pluripotent hematopoietic stem cells have been studied extensively, but

the events that occur during their differentiation remain largely uncharted. To develop a system that allows the differentiation of cultured multipotent progenitors by time-lapse fluorescence microscopy, myelomonocytic cells were labeled with green fluorescent protein (GFP) in vivo. This was achieved by knocking the enhanced GFP (EGFP) gene into the murine lysozyme M (lys) locus and using a targeting vector, which contains a neomycin resistant (neo) gene flanked by LoxP sites and 'splinked' ends, to increase the frequency of homologous recombination. Analysis of the blood and bone marrow of the lys- EGFP mice revealed that most myelomonocytic cells, especially mature neutrophil granulocytes, were fluorescence-positive, while cells from other lineages were not. Removal of the neo gene through breeding of the mice with the Cre-deleter strain led to an increased fluorescence intensity. Mice with an inactivation of both copies of the lys gene developed normally and were fertile. (C) 2000 by The American Society of Hematology.

AN 1999344567 EMBASE
TI Preferential liver irradiation enhances hematopoiesis through a thrombopoietin-independent mechanism.
AU Mouthon, Marc-Andre (correspondence); Vandamme, Marie; Gourmelon, Patrick
CS Inst. de Protect. et de Surete Nucl., IPSN B.P. no. 6, F-92265 Fontenay-aux-Roses Cedex, France.
AU Vainchenker, William; Wendling, Francoise
CS INSERM U362, Institut Gustave Roussy, F-94805, Villejuif Cedex, France.
AU Mouthon, Marc-Andre (correspondence)
CS Institut Protection/Surete Nucleaire, IPSN B.P. no. 6, F-92265 Fontenay-aux-Roses Cedex, France.
SO Radiation Research, (Oct 1999) Vol. 152, No. 4, pp. 390-397. Refs: 45
ISSN: 0033-7587 CODEN: RAREAE
CY United States
DT Journal; Article
FS 025 Hematology
046 Environmental Health and Pollution Control
048 Gastroenterology

LA English
SL English
ED Entered STN: 21 Oct 1999
Last Updated on STN: 21 Oct 1999
AB Liver synthesizes thrombopoietin, which is a major cytokine involved in
the production of hematopoietic cells. The purpose of this study was to
examine the effects of preferential liver irradiation on expression of
thrombopoietin and production of hematopoietic cells. About 70% of the
liver of C57BL6/J mice was irradiated with 20 Gy of γ rays.
Exposure to ionizing radiation enhanced hematopoietic progenitors and
megakaryocyte frequency in bone marrow and induced a transient increase in
platelet and neutrophil counts that peaked 14 days after irradiation. The
concentration of thrombopoietin was increased in serum as early as 5 h
after liver irradiation and was still elevated at day 14. By using
Northern blot analysis and an RNase protection assay, we showed that
thrombopoietin mRNA was increased in the irradiated liver. To determine
whether thrombopoietin was involved in the stimulation of hematopoiesis,
we irradiated mice in which thrombopoietin deficiency had been induced by
homologous recombination. Platelet levels were
increased in both heterozygous and homozygous thrombopoietin-deficient
mice with a magnitude similar to that obtained in normal mice. In
summary, our data demonstrate that local irradiation of the abdomen
encompassing the liver leads to stimulation of hematopoiesis through a
thrombopoietin-independent mechanism.

L21 ANSWER 18 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
reserved on STN
AN 1999201541 EMBASE
TI Expression of the transcription factor GATA-3 is required for the
development of the earliest T cell progenitors and correlates with stages
of cellular proliferation in the thymus.
AU Hendriks, Rudolf W. (correspondence); Van Doorninck, Hikke; Grosveld,

Frank; Karis, Alar
CS Dept. of Cell Biology and Genetics, Faculty of Medicine, Erasmus University Rotterdam, Rotterdam, Netherlands. hendriks@immu.fgg.eur.nl; hendricks@immu.fgg.eur.nl
AU Hendriks, Rudolf W. (correspondence); Nawijn, Martijn C.
CS Department of Immunology, Faculty of Medicine, Erasmus University Rotterdam, Dr. Molewaterplein 50, 3000 DR Rotterdam, Netherlands. hendriks@immu.fgg.eur.nl; hendricks@immu.fgg.eur.nl
AU Engel, J. Douglas
CS Department of Biochemistry, Molecular Biology and Cell Biology, Northwestern University, Evanston, IL, United States.
AU Karis, Alar
CS Inst. of Molecular and Cell Biology, University of Tartu, 23 Riia St., 51010 Tartu, Estonia.
SO European Journal of Immunology, (1999) Vol. 29, No. 6, pp. 1912-1918.
Refs: 24
ISSN: 0014-2980 CODEN: EJIMAF
CY Germany
DT Journal; Article
FS 021 Developmental Biology and Teratology
026 Immunology, Serology and Transplantation
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 1 Jul 1999
Last Updated on STN: 1 Jul 1999
AB GATA-3 is a zinc-finger transcription factor that is essential for both early T cell development and Th2 cell differentiation. To quantify GATA-3 expression during T cell development in vivo in the mouse, the GATA-3 gene was targeted by insertion of a lacZ reporter by homologous recombination in embryonic stem (ES) cells. Although we could detect GATA-3(+) cells throughout T cell development in the thymus, the proportions of GATA-3(+) cells varied considerably between the distinct differentiation stages. The two periods of TCR α and β gene recombination, which occur in quiescent or slowly dividing cells, were associated with low proportions of GATA-3(+) cells. Conversely, the stage of rapidly proliferating cells, which insulates these two waves of TCR rearrangement, was characterized by a large proportion of GATA-3(+) cells. In addition, we generated chimeric mice by injection of GATA-3-deficient

lacZ-expressing ES cells into wild-type blastocysts. In this in vivo
competition analysis, no contribution of GATA-3-deficient cells to the T
cell lineage was detected, not even in the earliest CD44(+)CD25(-)
double-negative (CD4(-)CD8(-)) cell stage in the thymus. These results
parallel data implicating other GATA family members as key regulators of
proliferation and survival of early hematopoietic cells. We therefore
propose that GATA-3 is required for the expansion of T cell progenitors,
and for the control of subsequent proliferation steps, which alternate
periods of TCR recombination in the thymus.

L21 ANSWER 19 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
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AN 1999046991 EMBASE
TI Permissive role of thrombopoietin and granulocyte colony-stimulating
factor receptors in hematopoietic cell fate decisions in vivo.
AU Stoffel, Ruedi; Ziegler, Sandra; Ghilardi, Nico; Skoda, Radek C.
(correspondence)
CS Biozentrum, University of Basel, Klingelbergstrasse 70, 4056 Basel,
Switzerland. skoda@ubaclu.unibas.ch
AU Ledermann, Birgit
CS Novartis Inc., P.O. Box, 4001 Basel, Switzerland.
AU De Sauvage, Frederic J.
CS Genentech Inc., Department of Oncology, 460 Point San Bruno Boulevard,
South San Francisco, CA 94080, United States.
SO Proceedings of the National Academy of Sciences of the United States of
America, (19 Jan 1999) Vol. 96, No. 2, pp. 698-702.
Refs: 34
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 021 Developmental Biology and Teratology
025 Hematology
LA English
SL English
ED Entered STN: 25 Feb 1999
Last Updated on STN: 25 Feb 1999
AB The question of whether extracellular signals influence hematopoiesis by
instructing stem cells to commit to a specific hematopoietic lineage

(instructive model) or solely by permitting the survival and proliferation
of predetermined progenitors (permissive model) has been controversial
since the discovery of lineage-dominant hematopoietic cytokines. To study
the potential role of cytokines and their receptors in hematopoietic cell
fate decisions, we used homologous recombination to
replace the thrombopoietin receptor gene (mpl) with a chimeric construct
encoding the extracellular domain of mpl and the cytoplasmic domain of the
granulocyte colony-stimulating factor receptor (G-CSFR). This chimeric
receptor binds thrombopoietin but signals through the G-CSFR intracellular
domain. We found that, despite the absence of a functional mpl signaling
domain, homozygous knock-in mice had a normal platelet count, indicating
that in vivo the cytoplasmic domain of G-CSFR can functionally replace mpl
signaling to support normal megakaryopoiesis and platelet formation. This
finding is compatible with the permissive model, according to which
cytokine receptors provide a nonspecific survival or proliferation signal,
and argues against an instructive role of mpl or G- CSFR in hematopoietic
cell fate decisions.

L21 ANSWER 20 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
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AN 1997351557 EMBASE
TI [New concepts on osteoclast origin: Relationship with normal and
inflammatory macrophages].
Nouveaux concepts sur l'origine des osteoclastes: Relation avec les
macrophages normaux et inflammatoires.
AU Solari, Florence (correspondence); Jurdic, Pierre
CS Lab. de Biol. Molec. et Cellulaire, UMR 49 Cnrs/Ens, Ecl. Normale Sup. de
Lyon, 46, allee d'Italie, 69364 Lyon Cedex 07, France.
AU Solari, Florence (correspondence)
CS Lab biologie moleculaire cellulaire, UMR 49 Cnrs-Ens, equipe Inra 913,
Ecole normale superieure de Lyon, 46 allee d'Italie, 69364 Lyon Cedex 07,
France.

SO Medecine/Sciences, (Nov 1997) Vol. 13, No. 11, pp. 1285-1293.
Refs: 47
ISSN: 0767-0974 CODEN: MSMSE4
CY France
DT Journal; General Review; (Review)
FS 025 Hematology
029 Clinical and Experimental Biochemistry
033 Orthopedic Surgery
LA French
SL French; English
ED Entered STN: 4 Dec 1997
Last Updated on STN: 4 Dec 1997
AB Osteoclasts are bone resorbing multinucleated giant cells. They derive from the fusion of hemopoietic mononucleated precursor cells, although their precise origin along the hemopoietic differentiation pathway is still a matter of discussion. Recent data obtained both in vivo and in vitro sustain the idea that osteoclasts derive from fusion of cells at the late stages of the monocytic pathway, or even directly from macrophages.
Osteoclasts, as well as macrophages, are phagocytic cells sharing in common many surface antigens. In vitro models have been developped enabling formation of osteoclasts directly from resident tissue microphages. Furthermore, analysis of osteopetrotic mice, obtained from either spontaneous mutations or after homologous recombinations, have shown that macrophages and osteoclasts are closely related. Finally, osteoclasts appear also to be highly related to polycaryonic macrophages found in inflammatory tissues. Here, we propose that only one way of differentiation leads from monocytes/macrophages to either inflammatory macrophages or bone resorbing osteoclasts, the final commitment depending upon microenvironment conditions.

L21 ANSWER 21 OF 24 EMBASE
AN 1997282875 EMBASE
TI A BCR-ABL(p190) fusion gene made by homologous recombination causes B- cell acute lymphoblastic leukemias in chimeric mice with independence of the endogenous bcr product.
AU Sanchez-Garcia, I., Dr. (correspondence)
CS Depto. Proliferacion y D., Inst. de Microbiol. Bioquim., Edificio

Departamental, Avda del Campo Charro s/n, 37007-Salamanca, Spain.
AU Castellanos, A.; Pintado, B.; Weruaga, E.; Arevalo, R.; Lopez, A.; Orfao, A.
AU Sanchez-Garcia, I., Dr. (correspondence)
CS DPDC, Inst. de Microbiologia Bioquimica, Edificio Departamental, Avda del Campo Charro s/n, 37007-Salamanca, Spain.
SO Blood, (15 Sep 1997) Vol. 90, No. 6, pp. 2168-2174.
Refs: 43
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; Article
FS 016 Cancer
022 Human Genetics
025 Hematology
LA English
SL English
ED Entered STN: 16 Oct 1997
Last Updated on STN: 16 Oct 1997
AB BCR-ABL(p190) oncogene is the result of a reciprocal translocation between chromosomes g and 22 and is associated with B-cell acute lymphoblastic leukemia (B-ALL) in humans. Current models expressing the BCR-ABL(p190) chimeric gene fail to consistently reproduce the phenotype with which the fusion gene is associated in human pathology, mainly due to the difficulty of being expressed in the appropriate cell type in vivo. We have used here homologous recombination in ES cells to create an in-frame fusion of BCR-ABL(p190)that mimics the consequences of the human chromosomal translocation by fusion of BCR-ABL coding sequences into the bcr endogenous gene. The chimeric mice generated with the mutant embryonic stem cells systematically develop B-ALL. Using these chimeric mice, we further show that BCR-ABL oncogene does not require the endogenous bcr product in leukemogenesis. Our results show that BCR-ABL(p190) chimeric mice are a new model to study the biology of the BCR-ABL oncogene and indicate the efficacy of this strategy for studying the role of specific chromosome abnormalities in tumor development.

L21 ANSWER 22 OF 24 EMBASE

reserved on STN
AN 1997200596 EMBASE
TI A 'knockdown' mutation created by cis-element gene targeting reveals the dependence of erythroid cell maturation on the level of transcription factor GATA-1.
AU McDevitt, M.A.; Shivdasani, R.A.; Fujiwara, Y.; Yang, H.; Orkin, S.H. (correspondence)
CS Division of Hematology/Oncology, Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, United States. orkin@rascal.med.harvard.edu
SO Proceedings of the National Academy of Sciences of the United States of America, (1997) Vol. 94, No. 13, pp. 6781-6785.
Refs: 32
ISSN: 0027-8424 CODEN: PNASA6
CY United States
DT Journal; Article
FS 001 Anatomy, Anthropology, Embryology and Histology
021 Developmental Biology and Teratology
025 Hematology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 31 Jul 1997
Last Updated on STN: 31 Jul 1997
AB The hematopoietic-restricted transcription factor GATA-1 is required for both mammalian erythroid cell and megakaryocyte differentiation. To define the mechanisms governing its transcriptional regulation, we replaced upstream sequences including a DNase 1 hypersensitive (HS) region with a neomycin- resistance cassette by homologous recombination in mouse embryonic stem cells and generated mice either harboring this mutation (neoΔHS) or lacking the selection cassette (ΔneoΔHS). Studies of the consequences of these targeted mutations provide novel insights into GATA-1 function in erythroid cells. First, the neoΔHS mutation leads to a marked impairment in the rate or efficiency of erythroid cell maturation due to a modest (4- to 5-fold) decrease in GATA-1 expression. Hence, erythroid differentiation is dose- dependent with respect to GATA-1. Second, since expression of GATA-1 from the ΔneoΔHS allele in erythroid cells is largely restored, transcription interference imposed by the introduced cassette must account for the 'knockdown' effect of the

mutation. Finally, despite the potency of the upstream sequences in
conferring high-level, developmentally appropriate expression of
transgenes in mice, other cis-regulatory elements within the GATA-1
compensate for its absence in erythroid cells. Our work illustrates the
usefulness of targeted mutations to create knockdown mutations that may
uncover important quantitative contribution of gene function not revealed
by conventional knockouts.

L21 ANSWER 23 OF 24 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
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AN 1996134420 EMBASE
TI CD34-deficient mice have reduced eosinophil accumulation after allergen
exposure and show a novel crossreactive 90-kD protein.
AU Suzuki, Akira, Dr. (correspondence)
CS Ontario Cancer Institute, Depts. of Med. Biophys. and Immunol., University
of Toronto, 620 University Ave, Toronto, Ont. M5G 2C1, Canada.
AU Andrew, David P.; Gonzalo, Jose-Angel; Fukumoto, Manabu; Spellberg, Jason;
Hashiyama, Motohiro; Takimoto, Hiroaki; Gerwin, Nicole; Webb, Lain;
Molineux, Graham; Amakawa, Ryuichi; Tada, Yoshifumi; Wakeham, Andrew;
Brown, John; McNiece, Ian; Ley, Klause; Butcher, Eugene C.; Suda, Toshio;
Gutierrez-Ramos, Jose-Carlos; Mak, Tak Wah
AU Suzuki, Akira, Dr. (correspondence)
CS Amgen Institute, Ontario Cancer Institute, University of Toronto, 620
University Ave, Toronto, Ont. M5G 2C1, Canada.
SO Blood, (1 May 1996) Vol. 87, No. 9, pp. 3550-3562.
Refs: 58
ISSN: 0006-4971 CODEN: BLOOAW
CY United States
DT Journal; Article
FS 026 Immunology, Serology and Transplantation
LA English
SL English
ED Entered STN: 20 May 1996
Last Updated on STN: 20 May 1996
AB CD34 is expressed on the surface of hematopoietic stem/progenitor cells,
stromal cells, and on the surface of high-endothelial venules (HEV). CD34
binds L-selectin, an adhesion molecule important for leukocyte rolling on

venules and lymphocyte homing to peripheral lymph nodes (PLN). We generated CD34-deficient mutant animals through the use of homologous recombination. Wild-type and mutant animals showed no differences in lymphocyte binding to PLN HEV, in leukocyte rolling on venules or homing to PLN, in neutrophil extravasation into peritoneum in response to inflammatory stimulus, nor in delayed type hypersensitivity. Anti-L-selectin monoclonal antibody (MEL-14) also inhibited these immune responses similarly in both CD34-deficient and wild-type mice. However, eosinophil accumulation in the lung after inhalation of a model allergen, ovalbumin, is several-fold lower in mutant mice. We found no abnormalities in hematopoiesis in adult mice and interactions between mutant progenitor cells and a stromal cell line in vitro were normal. No differences existed in the recovery of progenitor cells after 5- fluorouracil treatment, nor in the mobilization of progenitor cells after granulocyte colony-stimulating factor treatment compared with wild-type animals. Surprisingly, although CD34 was not expressed in these mice, a portion of its 90-kD band crossreactive with MECA79 remained after Western blot. Thus, we have identified an additional molecule(s) that might be involved in leukocyte trafficking. These results indicate that CD34 plays an important role in eosinophil trafficking into the lung.

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AN 1995209723 EMBASE

TI Failure of blood-island formation and vasculogenesis in Flk-1 deficient mice.

AU Shalaby, F.; Rossant, J. (correspondence); Yamaguchi, T.P.; Gertsenstein, M.; Wu, X.-F.; Breitman, M.L.; Schuh, A.C.

CS Samuel Lunenfeld Research Institute, Mount Sinai Hospital, 600 University Avenue, Toronto, Ont. M5G 1X5, Canada.

SO Nature, (1995) Vol. 376, No. 6535, pp. 62-66.

ISSN: 0028-0836 CODEN: NATUAS
CY United Kingdom
DT Journal; Article
FS 001 Anatomy, Anthropology, Embryology and Histology
021 Developmental Biology and Teratology
025 Hematology
LA English
SL English
ED Entered STN: 3 Aug 1995
Last Updated on STN: 3 Aug 1995
AB The receptor tyrosine kinase Flk-1 is believed to play a pivotal role in endothelial development. Expression of the Flk-1 receptor is restricted to endothelial cells and their embryonic precursors, and is complementary to that of its ligand, vascular endothelial growth factor (VEGF), which is an endothelial-specific mitogen. Highest levels of flk-1 expression are observed during embryonic vasculogenesis and angiogenesis, and during pathological processes associated with neovascularization, such as tumour angiogenesis. Because flk-1 expression can be detected in presumptive mesodermal yolk-sac blood-island progenitors as early as 7.0 days postcoitum, Flk-1 may mark the putative common embryonic endothelial and haematopoietic precursor, the haemangioblast, and thus may also be involved in early haematopoiesis. Here we report the generation of mice deficient in Flk-1 by disruption of the gene using homologous recombination in embryonic stem (ES) cells. Embryos homozygous for this mutation die in utero between 8.5 and 9.5 days post-coitum, as a result of an early defect in the development of haematopoietic and endothelial cells. Yolk-sec blood islands were absent at 7.5 days, organized blood vessels could not lie observed in the embryo or yolk sac at any stage, and haematopoietic progenitors were severely reduced. These results indicate that Flk-1 is essential for yolk-sac blood-island formation and vasculogenesis in the mouse embryo.

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COST IN U.S. DOLLARS SINCE FILE TOTAL

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                                                        ENTRY    SESSION
FULL ESTIMATED COST                                    212.37     212.59

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                        ENTRY    SESSION
CA SUBSCRIBER PRICE                                     -5.74
-5.74

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LAST RELOADED: Jan  6, 2009 (20090106/UP).

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COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                     1.89     214.48

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                        ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00
-5.74

STN INTERNATIONAL LOGOFF AT 18:42:56 ON 07 JAN 2009


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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2
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 NEWS  1            Web Page for STN Seminar Schedule - N. America
 NEWS  2  DEC 01    ChemPort single article sales feature unavailable
 NEWS  3  JAN 06    The retention policy for unread STNmail messages
                    will change in 2009 for STN-Columbus and STN-Tokyo
 NEWS  4  JAN 07    WPIDS, WPINDEX, and WPIX enhanced Japanese Patent
                    Classification Data
 NEWS  5  FEB 02    Simultaneous left and right truncation (SLART) added
                    for CERAB, COMPUAB, ELCOM, and SOLIDSTATE
 NEWS  6  FEB 02    GENBANK enhanced with SET PLURALS and SET SPELLING
 NEWS  7  FEB 06    Patent sequence location (PSL) data added to USGENE
 NEWS  8  FEB 10    COMPENDEX reloaded and enhanced
 NEWS  9  FEB 11    WTEXTILES reloaded and enhanced
 NEWS 10  FEB 19    New patent-examiner citations in 300,000 CA/CAplus
                    patent records provide insights into related prior
                    art
 NEWS 11  FEB 19    Increase the precision of your patent queries -- use
                    terms from the IPC Thesaurus, Version 2009.01
 NEWS 12  FEB 23    Several formats for image display and print options
                    discontinued in USPATFULL and USPAT2
 NEWS 13  FEB 23    MEDLINE now offers more precise author group fields
                    and 2009 MeSH terms
 NEWS 14  FEB 23    TOXCENTER updates mirror those of MEDLINE - more
                    precise author group fields and 2009 MeSH terms
 NEWS 15  FEB 23    Three million new patent records blast AEROSPACE
into
                    STN patent clusters
 NEWS 16  FEB 25    USGENE enhanced with patent family and legal status
                    display data from INPADOCDB
 NEWS 17  MAR 06    INPADOCDB and INPAFAMDB enhanced with new display
                    formats
 NEWS 18  MAR 11    EPFULL backfile enhanced with additional full-text
                    applications and grants
 NEWS 19  MAR 11    ESBIOBASE reloaded and enhanced
 NEWS 20  MAR 20    CAS databases on STN enhanced with new super role
                    for nanomaterial substances
 NEWS 21  MAR 23    CA/CAplus enhanced with more than 250,000 patent
                    equivalents from China
 NEWS 22  MAR 30    IMSPATENTS reloaded and enhanced
 NEWS 23  APR 03    CAS coverage of exemplified prophetic substances
                    enhanced
 NEWS 24  APR 07    STN is raising the limits on saved answers

 NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,
              AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

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 NEWS IPC8      For general information regarding STN implementation
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FILE 'HOME' ENTERED AT 14:59:11 ON 20 APR 2009

=> FIL BIOSIS CAPLUS EMBASE
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                       0.22       0.22

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FILE 'EMBASE' ENTERED AT 14:59:20 ON 20 APR 2009
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=> s multipotent adult stem cell or MAPC
L1          348 MULTIPOTENT ADULT STEM CELL OR MAPC

=> s l1 and homologous recombin?
L2            3 L1 AND HOMOLOGOUS RECOMBIN?

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3            2 DUP REM L2 (1 DUPLICATE REMOVED)

=> d bib abs 1-y
'ACC' IS NOT VALID WITH MULTIFILE PROCESSING

DISPLAY ACC is not allowed in a multifile environment.  Enter
"DISPLAY HISTORY" to locate the file the L# was created in, use the
FILE command to enter that file, and re-enter the DISPLAY ACC
command.
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=> d bib abs 1-
YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):y

L3   ANSWER 1 OF 2  BIOSIS  COPYRIGHT (c) 2009 The Thomson
Corporation  on STN
     DUPLICATE 1
AN   2008:88063  BIOSIS
DN   PREV200800088197
TI   Stem cells and embryonic stem cells: Biological differences.
     Original Title: Celulas madre y celulas troncoembrionarias:
Diferencias
     biologicas.
AU   Riveros, Dolly Macias [Reprint Author]; Vazquez Chagoyan, Juan
Carlos;
     Morales, Rogelio Alonso; Juarez, Marco Cajero
CS   Univ Autonoma Estado Mexico, Fac Med Vet and Zootecnia, Program
Estudios
     Avanzados Salud Anim, Km 15 5, Mexico City, DF, Mexico
     marmac4@uaemex.mx; jcvc@uaemex.mx; ralonsom@servidor.unam.mx;
     cajeromarco@hotmail.com
SO   Veterinaria Mexico, (OCT-DEC 2007) Vol. 38, No. 4, pp. 477-501.
     CODEN: VTERBU. ISSN: 0301-5092.
DT   Article
LA   Spanish
ED   Entered STN: 23 Jan 2008
     Last Updated on STN: 23 Jan 2008
AB   The stem cells have been classified in three types according to
their
     natural nicheof origin, aptitude and differential function:
totipotential,
     pluripotential and multipotential; the first, called embryonic
stem cells
     (ES) originate from the morulae; the second, come from the inner
cell mass
     of the blastocyst (ICM); and the third, known as multipotent
adult
     progenitor cells (MAPC are found in some adult tissues.  The
     biological difference lies in their capabilities to produce cell
lines,
     the totipotentials have the faculty to originate a complete
organism, the
     pluripotential can generate all the cellular types and even the
germinal
     line and the multipotentials can derivate in specific lineages.
The stem
     cells are able to self-renew, and originate daughter-cells
compromised
     with certain development routes; they are characterized for their
     indefinite division and are morphologically and functionally
     differentiated.  When the stem cells and some progenitor types
are
     extracted from their natural environment and are grown in vitro,
in
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suitable medium, can be transfected and remain in an undifferentiated
state without losing their potentiality; thus, when they are reintegrated
to blastocyst receptors they are able to go on with their development.
The study and compilation of information about these biological qualities
of differential function, as well as their usefulness in
homologous recombination and production of animal models
that generate recombinant proteins, applicable for preventive-regenerating
medicine and treatment of diseases, constitute the aim of this work.

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:493864 CAPLUS
DN 141:66248
TI Homologous recombination in multipotent adult progenitor cells
IN Verfaillie, Catherine; Lakshmipathy, Uma
PA Regents of the University of Minnesota, USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004050859	A2	20040617	WO 2003-US38811	20031125
	WO 2004050859	A3	20040812		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,

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            TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG
     AU 2003298016        A1    20040623    AU 2003-298016
20031125
     US 20060228798       A1    20061012    US 2006-536716
20060530
PRAI US 2002-429631P      P     20021127
     WO 2003-US38811      W     20031125
AB   The invention relates to methods of altering gene expression by
     homologous recombination in a multipotent adult
     progenitor cell (MAPC).  In particular, methods of producing a
     recombinant MAPC, of correcting a genetic defect in a mammal, of
     providing a functional and/or therapeutic protein to a mammal,
and of
     transforming and differentiating a MAPC are provided.  MAPCs
     containing an exogenous DNA as well as recombinant MAPCs and
their
     differentiated progeny are also provided.  The examples disclose
gene
     targeting and genetic correction of a mutation in the FANCC
protein,
     involved in Fanconi anemia, in mouse MAPCs, followed by
transplantation of
     the corrected cells into FANCC-/- mouse and subsequent reversal
of the FANCC
     deficiency.


=> d his

     (FILE 'HOME' ENTERED AT 14:59:11 ON 20 APR 2009)

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:59:20 ON 20 APR 2009
L1          348 S MULTIPOTENT ADULT STEM CELL OR MAPC
L2            3 S L1 AND HOMOLOGOUS RECOMBIN?
L3            2 DUP REM L2 (1 DUPLICATE REMOVED)

=> s l1 and review
L4          24 L1 AND REVIEW

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5           17 DUP REM L4 (7 DUPLICATES REMOVED)

=> d bib abs 1-
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L5   ANSWER 1 OF 17  BIOSIS  COPYRIGHT (c) 2009 The Thomson
Corporation  on STN
     DUPLICATE 1
AN   2008:636521  BIOSIS
DN   PREV200800636520
```

TI Multipotent adult progenitor cells: their role in wound healing and the
treatment of dermal wounds.
AU Herdrich, B. J.; Lind, R. C.; Liechty, K. W. [Reprint Author]
CS Abramson Res Bldg,3615 Civ Ctr Blvd,Rm 1116E, Philadelphia, PA 19104 USA
Liechty@email.chop.edu
SO Cytotherapy, (2008) Vol. 10, No. 6, pp. 543-550.
ISSN: 1465-3249.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 19 Nov 2008
Last Updated on STN: 27 Nov 2008
AB The use of cellular therapy in the treatment of dermal wounds is currently
an active area of investigation. Multipotent adult progenitor cells (
MAPC) are an attractive choice for cytotherapy because they have a
large proliferative potential, the ability to differentiate into different
cell types and produce a variety of cytokines and growth factors important
to wound healing. Whole bone marrow (BM) was one of the initial attempts
to treat impaired wounds. While it has shown some promise, the low
frequency of progenitor cell populations in BM and the large number of
inflammatory cells make it less attractive. Multipotent mesenchymal
stromal cells (MSC) and endothelial progenitor cells are populations of
BM-derived progenitor cells that have been isolated and used to treat
chronic wounds with some success. Skin-derived MAPC are another
heterogeneous population of progenitor cells present in the skin with the
potential to differentiate into skin elements and participate in wound
healing. All of these progenitor cell populations are potential sources
for cytotherapy of wounds. This review focused on the
contribution of adult progenitor cell populations to dermal wound healing
and their potential for use in cytotherapy.

L5 ANSWER 2 OF 17 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
DUPLICATE 2
AN 2008:383052 BIOSIS

DN PREV200800383051
TI Bone marrow - Home of versatile stem cells.
AU Ratajczak, Mariusz Z. [Reprint Author]; Zuba-Surma, Ewa K.; Wojakowski,
Wojtek; Ratajczak, Janina; Kucia, Magda
CS Univ Louisville, Stem Cell Inst, James Graham Brown Canc Ctr, 500 S Floyd
St, Louisville, KY 40202 USA
mzrata01@louisville.edu
SO Transfusion Medicine and Hemotherapy, (2008) Vol. 35, No. 3, pp. 248-259.
ISSN: 1660-3796.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 9 Jul 2008
Last Updated on STN: 9 Jul 2008
AB Bone marrow (BM) has been for many years primarily envisioned as the 'home
organ' of hematopoietic stem cells (HSC). In this review we
will discuss current views of the BM stem cell compartment and present
data showing that BM in addition to HSC also contains a heterogeneous
population of non-hematopoietic stem cells. These cells have been
variously described in the literature as i) endothelial progenitor cells
(EPC), ii) mesenchymal stem cells (MSC), iii) multipotent adult progenitor
cells (MAPC), iv) marrow-isolated adult multilineage inducible
(MIAMI) cells, v) multipotent adult stem cells (MACS) and vi) very small
embryonic-like (VSEL) stem cells. It is likely that in many cases similar
or overlapping populations of primitive stem cells in the BM were detected
using different experimental strategies and hence were assigned different
names.

L5 ANSWER 3 OF 17 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
reserved on STN
AN 2008593071 EMBASE
TI Purification and culture of human blood vessel-associated progenitor
cells.
AU Crisan, Mihaela (correspondence); Huard, Johnny; Sun, Bin; Yap, Solomon;
Giacobino, Jean-Paul; Casteilla, Louis; Peault, Bruno
CS Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, United States.

AU Huard, Johnny; Peault, Bruno
CS McGowan Institute for Regenerative Medicine, Pittsburgh, PA, United States
.
AU Zheng, Bo; Logar, Alison; Giacobino, Jean-Paul
CS Department of Orthopedic Surgery and Molecular Genetics and Biochemistry,
Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, United States.
AU Crisan, Mihaela (correspondence); Huard, Johnny; Zheng, Bo; Sun, Bin; Yap,
Solomon; Logar, Alison; Giacobino, Jean-Paul; Peault, Bruno
CS Stem Cell Research Center, Children's Hospital of Pittsburgh of UPMC,
Pittsburgh, PA, United States.
AU Yap, Solomon
CS University of Pittsburgh, Pittsburgh, PA, United States.
AU Casteilla, Louis
CS University of Toulouse, Toulouse, France.
SO Current Protocols in Stem Cell Biology, (2008) No. SUPPL. 4, pp. 2B.2.1-2B.2.13.
Refs: 20
ISSN: 1938-8969 E-ISSN: 1941-7322
PB John Wiley and Sons Inc., 111 River Street, Hoboken, NJ 07030-5774, United
States.
CY United States
DT Journal; General Review; (Review)
FS 029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 16 Jan 2009
Last Updated on STN: 16 Jan 2009
AB Multilineage progenitor cells, diversely designated as MSC, MAPC
, or MDSC, have been previously extracted from long-term cultures of fetal
and adult organs (e.g., bone marrow, brain, lung, pancreas, muscle,
adipose tissue, and several others). The identity and location, within
native tissues, of these elusive stem cells are described here. Subsets
of endothelial cells and pericytes, which participate in the architecture
of human blood vessels, exhibit, following purification to homogeneity,
developmental multipotency. The selection from human tissues, by flow
cytometry using combinations of positive and negative cell surface
markers, of endothelial and perivascular cells is described here. In

addition, a rare subset of myoendothelial cells that express markers of both endothelial and myogenic cell lineages and exhibit dramatic myogenic and cardiomyogenic potential has been identified and purified from skeletal muscle. The culture conditions amenable to the long-term proliferation of these blood vessel-associated stem cells in vitro are also described. .COPYRGT. 2008 by John Wiley & Sons, Inc.

L5 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2008:88774 CAPLUS
DN 148:324783
TI Stem cells and embryonic stem cells: biological differences
AU Riveros, Dolly Macias; Chagoyan, Juan Carlos Vazquez; Morales, Rogelio Alonso; Juarez, Marco Cajero
CS Programa de Estudios de Posgrado, Facultad de Medicina Veterinaria y Zootecnia, Universidad Autonoma del Estado de Mexico, Mexico City, Mex.
SO Veterinaria Mexico (2007), 38(4), 477-501
CODEN: VTERBU; ISSN: 0301-5092
PB Facultad de Medicina Veterinaria y Zootecnia de la Universidad Nacional Autonoma de Mexico
DT Journal; General Review
LA English/Spanish
AB A review. The stem cells have been classified in three types according to their natural niche of origin, aptitude and differential function: totipotential, pluripotential and multipotential; the first, called embryonic stem cells (ES) originate from the morulae; the second, come from the inner cell mass of the blastocyst (ICM); and the third, known as multipotent adult progenitor cells (MAPC) are found in some adult tissues. The biol. difference lies in their capabilities to produce cell lines, the totipotentials have the faculty to originate a complete organism, the pluripotential can generate all the cellular types and even the germinal line and the multipotentials can derivate in specific lineages. The stem cells are able to self-renew, and originate daughter-cells compromised with certain development routes; they are

characterized for their indefinite division and are morphol. and functionally differentiated. When the stem cells and some progenitor types are extracted from their natural environment and are grown in vitro, in suitable medium, can be transfected and remain in an undifferentiated state without losing their potentiality; thus, when they are reintegrated to blastocyst receptors they are able to go on with their development. The study and compilation of information about these biol. qualities of differential function, as well as their usefulness in homologous recombination and production of animal models that generate recombinant proteins, applicable for preventive-regenerating medicine and treatment of diseases, constitute the aim of this work.
RE.CNT 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:511777 CAPLUS
DN 147:284597
TI Novel angiogenic therapy using tissue stem cells and materials engineering
AU Sata, Masataka
CS Grad. Sch. of Medicine, The Univ. of Tokyo, Tokyo, Japan
SO Therapeutic Research (2007), 28(3), 325-331
CODEN: THREEL; ISSN: 0289-8020
PB Raifu Saiensu Shuppan K.K.
DT Journal; General Review
LA Japanese
AB A review. Stem cells are a kind of special cells with the ability of self renewing and differentiation and mainly located in the marrow. More and more researches have proved that stem cells are related to the tissue repair. Recent research has found that multipotent adult stem cell is also related to distant blood vessel repair, remodeling and disease formation. Bone marrow cell is mobilized and fixed in injured vessel as circulating precursor cell to differentiate smooth muscle cell and endothelial cell. This maybe the new therapeutic target for angiopathy. This dissertation introduced the most novel angiogenic therapy using tissue stem cells and materials engineering. The novel angiogenic therapy includes two main parts: one is

creation of bio-artificial blood vessel by using blood vessel precursor
cell and the other is novel angiogenic therapy using tissue stem cells and
low mol. compound

L5 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:477682 CAPLUS
DN 147:68870
TI Organogenesis and tissue regeneration using bone marrow stem cells
AU Oki, Masayuki; Ando, Kiyoshi
CS Sch. of Medicine, Dep. of Internal Medicine, Tokai Univ., Japan
SO Annual Review Ketsueki (2007) 46-54
CODEN: ARKNB7
PB Chugai Igakusha
DT Journal; General Review
LA Japanese
AB A review. The topics discussed are (1) plasticity and
pluripotency of stem cells; (2) types of stem cells in the bone marrow
including mesenchymal stem cells (MSC), multipotent adult progenitor cells
(MAPC) and hematopoietic stem cells; and (3) tissue regeneration
of heart, nerve, bone, liver and blood using MSC and MAPC.

L5 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:792443 CAPLUS
DN 146:248292
TI Impairment of the activity of glycosaminoglycan-binding cytokines by
functionally abnormal heparan sulfates: a novel mechanism underlying
disease pathophysiology
AU Gupta, Pankaj
CS Hematology/Oncology Section, Veterans Affairs Medical Center &
Hematology-Oncology-Transplantation Division, Department of Medicine,
University of Minnesota Medical School, Minneapolis, USA
SO TheScientificWorld (2006), 6(Jan.), 452-456
CODEN: THESAS; ISSN: 1532-2246
URL:
http://www.thescientificworld.com/headeradmin/upload/2006.21.83.pdf
PB TheScientificWorld, Inc.
DT Journal; General Review; (online computer file)
LA English
AB A review. Multipotent adult progenitor cell (MAPC)
derived from normal donors and patients with Hurler syndrome was used to
examine the structure and the functional properties of Hurler heparan
sulfate. Using metabolic labeling of glycosaminoglycans (GAGs), the HS

that accumulates in Hurler MAPC contained a large proportion of small polysaccharide chains. HPLC of fluorescently labeled disaccharides showed that the disaccharide composition of accumulated HS in Hurler MAPC was also markedly abnormal. While both normal and Hurler HS were compromised of the six major disaccharide types, the proportions of all three 6-O-sulfated disaccharides were lower in Hurler HS. There was a progressive decline in the proportion of UAGlcNS6S with increasing total accumulation of GAGS. This novel observation suggests that the structural aberration of HS in Hurler syndrome may continue to worsen with progression of the disease.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 17 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
DUPLICATE 3
AN 2005:318395 BIOSIS
DN PREV200510104054
TI Bone marrow as a home of heterogenous populations of nonhematopoietic stem cells.
AU Kucia, M.; Reca, R.; Jala, V. R.; Dawn, B.; Ratajczak, J.; Ratajczak, M.
Z. [Reprint Author]
CS Univ Louisville, Stem Cell Biol Program, James Graham Brown Canc Ctr, Louisville, KY 40202 USA
mzrata01@louisville.edu
SO Leukemia (Basingstoke), (JUL 2005) Vol. 19, No. 7, pp. 1118-1127.
CODEN: LEUKED. ISSN: 0887-6924.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 17 Aug 2005
Last Updated on STN: 17 Aug 2005
AB Evidence is presented that bone marrow (BM) in addition to CD45(positive) hematopoietic stem cells contains a rare population of heterogenous CD45(negative) nonhematopoietic tissue committed stem cells (TCSC). These nonhematopoietic TCSC (i) are enriched in population of CXCR4(+) CD34(+) AC133(+) lin(-) CD45(-) and CXCR4(+) Sca-1(+) lin(-) CD45(-) in humans and

mice, respectively, (ii) display several markers of pluripotent stem cells (PSC) and (iii) as we envision are deposited in BM early in development. Thus, since BM contains versatile nonhematopoietic stem cells, previous studies on plasticity trans-dedifferentiation of BM-derived hematopoietic stem cells (HSC) that did not include proper controls to exclude this possibility could lead to wrong interpretations. Therefore, in this spotlight review we present this alternative explanation of 'plasticity' of BM-derived stem cells based on the assumption that BM stem cells are heterogenous. We also discuss a potential relationship of TCSC/PSC identified by us with other BM-derived CD45(negative) nonhematopoietic stem cells that were recently identified by other investigators (eg MSC, MAPC, USSC and MIAMI cells). Finally, we discuss perspectives and pitfalls in potential application of these cells in regenerative medicine.

L5 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:154226 CAPLUS
DN 145:59671
TI Adult stem cells and possible mechanisms of its differentiation-editorial
AU Zhou, Zhuoyan; Yang, Mo; Jiang, Yuehua
CS Medical College, Jinan University, Guangzhou, 510632, Peop. Rep. China
SO Zhongguo Shiyan Xueyexue Zazhi (2005), 13(3), 353-357
CODEN: ZSXZAF; ISSN: 1009-2137
PB Zhongguo Shiyan Xueyexue Zazhishe
DT Journal; General Review
LA Chinese
AB A review. Adult stem cells are the multi-potential cells, which exist in fetal and adult tissues. It can reproduce itself (undergo self-renewal) or give rise to more specialized (differentiated) cells. Under certain inducing conditions, adult stem cells can acquire the ability to differentiate into different tissue cells. Multipotent adult progenitor cells (MAPC), an alternative name of adult stem cell given by Catherine Verfaillie, existing in bone marrow, can differentiate into cells with characteristics of mesodermal, neuroectodermal, and

endodermal lineages in vitro at the single-cell level. MAPC can also contribute to most cell types when injected into the blastocyst.

Adult stem cell differentiation implies that different cell lineages are derived from a single initial cell. All differentiated cell types are functional in vitro and in vivo and engraftment is robust and persistent in the physiol. and pathol. situations. The possible mechanisms may underlie the differentiation: various tissue-specific stem cells are present in different niche that imparts signals to activate a novel genetic program needed for the new cell fate. And true multi-potential stem cells persist in postnatal life. In the future, multi-potent adult stem cells might then be used for therapies of degenerative or genetic disorders of multiple different organs.

L5 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 4
AN 2004:1064432 CAPLUS
DN 142:131212
TI Stem cells today: B1. bone marrow stem cells
AU Edwards, Bob
CS Reproductive BioMedicine Online, Dray Drayton, Cambridge, CB3 8DB, UK
SO Reproductive BioMedicine Online (2004), 9(5), 541-583
CODEN: RBOEA6; ISSN: 1472-6483
PB Reproductive Healthcare Ltd.
DT Journal; General Review
LA English
AB A review. This is the 2nd in a series of 4 devoted to the anal. of recent studies on stem cells. The 1st considered embryo stem cells (ES). This review covers bone marrow stem cells. They are analyzed initially in a historical perspective, and then in relation to foundation studies in the later 20th century before a detailed anal. is presented on very recent studies. Methods of identifying, culturing, expanding and grafting stem cells are described, including the separation of hemopoietic and mesenchyme cell lines (HSC and MSC) and recent more detailed analyses using numerous CD and other markers to identify very small subsets of stem cells such as multipotent adult progenitor cells (

MAPC) and bone marrow stromal stem cells (BMSSC) from MSC.
Queries arising on the immense potential of these stem cell lines due to
the discovery of epigenetic factors and cell fusions influencing their
development and potency are described. A section on cord blood stem cells
is followed by a detailed discussion on the modern situation regarding the
clin. use of stem cells, its recent setbacks due to epigenetic factors,
different approaches to the discovery of a highly multipotent bone marrow
stem cell, and a brief description of embryol. approaches to identifying
the basic bone marrow stem cell in very early mammalian embryos.
RE.CNT 195 THERE ARE 195 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 11 OF 17 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 5
AN 2004:322633 BIOSIS
DN PREV200400323444
TI Bone and fat - Old questions, new insights.
AU Gimble, Jeffrey M. [Reprint Author]; Nuttal, Mark E.
CS Pennington Biomed Res CtrStem Cell Lab, Louisiana State Univ, 6400 Perkins
Rd, Baton Rouge, LA, 70808, USA
gimblejm@pbrc.edu
SO Endocrine, (March 2004) Vol. 23, No. 2-3, pp. 183-188. print.
ISSN: 1355-008X.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 21 Jul 2004
Last Updated on STN: 21 Jul 2004
AB Until recently, adipose tissue was considered to serve only as a triglyceride reservoir and was relegated to a passive endocrine role.
With the discovery of leptin and other adipokines, adipose tissue is now
recognized as an active participant in systemic metabolism. This
review focuses on the complex relationship existing between
adipose tissue and bone metabolism and differentiation. It explores the
paradigms that have shaped the past decade's research and what these
findings forecast for the future. Particular attention is given to the
multipotent adult stem cell
populations that reside within bone and fat. These adult stem cells have

critical importance to the emerging field of tissue engineering and
regenerative medicine.

L5 ANSWER 12 OF 17 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 6
AN 2004:386407 BIOSIS
DN PREV200400386308
TI Heterogeneous populations of bone marrow stem cells - are we spotting on
the same cells from the different angles?.
AU Ratajczak, Mariusz Z. [Reprint Author]; Kucia, Magda; Majka, Marcin; Reca,
Ryan; Ratajczak, Janina
CS James Graham Brown Canc CtrStem Cell Biol Program, Univ Louisville, 529 S
Jackson St, Louisville, KY, 40202, USA
mzrata01@louisville.edu
SO Folia Histochemica et Cytobiologica, (2004) Vol. 42, No. 3, pp. 139-146.
print.
CODEN: FHCYEM. ISSN: 0239-8508.
DT Article
General Review; (Literature Review)
LA English
ED Entered STN: 29 Sep 2004
Last Updated on STN: 29 Sep 2004
AB Accumulated evidence suggests that in addition to hematopoietic stem cells
(HSC), bone marrow (BM) also harbors endothelial stem cells (ESC),
mesenchymal stem cells (MSC), multipotential adult progenitor cells (
MAPC), pluripotent stem cells (PCS) as well as tissue committed
stem cells (TCSC) recently identified by us. In this review we
discuss the similarities and differences between these cell populations.
Furthermore, we will present the hypothesis that all of these versatile BM
derived stem cells are in fact different subpopulations of TCSC. These
cells accumulate in bone marrow during ontogenesis and being a mobile
population of cells are released from BM into peripheral blood after
tissue injury to regenerate damaged organs. Furthermore, since BM is a
"hideout" for TCSC, their presence in preparations of bone marrow derived
mononuclear cells should be considered before experimental evidence is

interpreted simply as trans-differentiation or plasticity of HSC. Finally, our observation that the number of TCSC accumulate in the bone marrow of young animals and their numbers decrease during senescence provides a new insight into aging and may explain why the regeneration processes becomes less effective in older individuals.

L5 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2004:339356 CAPLUS
DN 140:388923
TI The bone marrow: a reserve of stem cells able to repair various tissues?
AU Cavazzana-Calvo, M.; Lagresle, C.; Andre-Schmutz, I.; Hacein-Bey-Abina, S.
CS Departement de biotherapie, Fr.
SO Annales de Biologie Clinique (2004), 62(2), 131-138
CODEN: ABCLAI; ISSN: 0003-3898
PB John Libbey Eurotext
DT Journal; General Review
LA French
AB A review. Hematopoietic stem cells (HSC) have been widely used for autologous and allogeneic transplantation during decades, although little was known about their migration, survival, self-renewal and differentiation process. Their sorting by the CD34+ marker they express at the cell surface in human has been challenged by the recent discovery of HSC in the CD34- compartment that may precede CD34+ HSC in the differentiation process. Until recently, stem cells present in the bone marrow were thought to be specific for hematopoiesis. Some expts. including clin. trials showing the formation of various tissues, muscle, neural cells and hepatocytes for instance, after transplantation of medullar cells, have challenged this dogma. In fact, the proofs of such a transdifferentiation process by HSC are still missing and the observations may result from the differentiation of other multipotent stem cells present in the bone marrow, such as mesenchymal stem cells and more primitive multi-potent adult progenitor cells (MAPC) and side population (SP) cells.
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 17 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
reserved on STN
AN 2003323882 EMBASE
TI [Plasticity of adult stem cells].
Plasticite des cellules souches adultes.
AU Turhan, Ali (correspondence)
CS U. de Therapie Cell. et Inserm U362, Institut Gustave-Roussy, 39, rue
Camille-Desmoulins, 94805 Villejuif Cedex, France. turali@igr.fr
SO Hematologie, (Mar 2003) Vol. 9, No. 2, pp. 105-116.
Refs: 66
ISSN: 1264-7527 CODEN: HEMAF2
CY France
DT Journal; General Review; (Review)
FS 025 Hematology
LA French
SL English; French
ED Entered STN: 28 Aug 2003
Last Updated on STN: 28 Aug 2003
AB During the recent years, experimental data obtained in the murin system
led to a drastic change in our classical concepts of adult stem cells.
Until recently, these cells, in addition to their classical self-renewal
and differentiation abilities, were supposed to exhibit
tissue-specificity. This concept has been challenged by bone marrow
transplantation experiments in demonstrating that not marrow cells could
generate not only hematopoietic cells but also muscle cells, hepatic cells
or neuronal cells in lethally irradiated recipients. Conversely, muscle
cells or brain cells could generate hematopoietic cells upon
transplantation. The term "plasticity" has been coined to explain this
phenomenon which could be due to the persistence in adult tissues, of stem
cells with multi-differentiation ability or to the "transdifferentiation"
ability of some adult cells committed to differentiation, under the
influence of some environmental cues, a phenomenon which is known to occur
in vitro. The phenotype of cells at the origin of
«plasticity» is currently the subject of investigations and
controversies in many laboratories. If the functional nature of several
types of cells generated after bone marrow transplantation has been

demonstrated in mice, experiments using clonal transplantations have given
conflicting results. The relationship of the cells at the origin of the
stem cells plasticity with a new type of mesodermal cell designed under
the term of "multipotent adult progenitor cell" (MAPC) remains
to be determined. The discovery of this latter is a major advance in this
field as the MAPC have isolated from the adult bone marrow and
present certain characteristics of embryonic stem cells with the
demonstration of their totipotency towards many tissues, including
hematopoiesis. The discovery of the adult stem cell plasticity phenomenon
in general, whether due to the programming of adult stem cells under the
influence of some specific environmental cues or to the persistence in
adult tissues of stem cells with embryonal characteristics, represent a
major change in our concepts of stem and developmental biology. Many in
vitro and in vivo experiments will be necessary to determine if the data
generated by the use of adults stem cells in mice could be translated to
humans in order to develop future cell therapy protocols.

L5 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:109123 CAPLUS
DN 136:291972
TI Putting the neo into neoangiogenesis
AU Moore, Malcolm A. S.
CS Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA
SO Journal of Clinical Investigation (2002), 109(3), 313-315
CODEN: JCINAO; ISSN: 0021-9738
PB American Society for Clinical Investigation
DT Journal; General Review
LA English
AB A review. The research of Reyes, M.; et al. (2002) on the
participation of endothelial cells in new blood vessel formation in normal
and pathol. states, including tumor neoangiogenesis, is reviewed with
commentary and refs. A unique cell in human and rodent postnatal marrow,
designated the multipotent adult progenitor cell (MAPC), was
identified. MAPCs were selected by depleting adult bone marrow of
hematopoietic cells expressing CD45 and glycophorin-A, followed by

long-term culture of fibronectin with EGF and PDGF under low serum conditions. The potential of human MAPCs , obtained after 20-65 PD, to form functional endothelium, was evaluated. The results showed that the cells form vascular tubes when plated on Matrigel and upregulate angiogenic receptors and VEGF in response to hypoxia. A comparison of MAPC with embryonic stem cells and cells generated by therapeutic cloning is presented.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:396338 CAPLUS
DN 137:319820
TI Bone marrow stromal cells as targets for gene therapy
AU Van Damme, An; Vanden Driessche, Thierry; Collen, Desire; Chuah, Marinee K. L.
CS Center for Transgene Technology and Gene Therapy, Flanders Interuniversity Institute for Biotechnology-University of Leuven, Louvain, B-3000, Belg.
SO Current Gene Therapy (2002), 2(2), 195-209
CODEN: CGTUAH; ISSN: 1566-5232
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
AB A review. The bone marrow (BM) is composed of the non-adherent hematopoietic and adherent stromal cell compartment. This adherent BM stromal cell fraction contains pluripotent mesenchymal stem cells (MSCs) and differentiated mesenchymal BM stromal cells. The MSCs self-renew by proliferation while maintaining their stem-cell phenotype and give rise to the differentiated stromal cells which belong to the osteogenic, chondrogenic, adipogenic, myogenic and fibroblastic lineages. A more primitive adherent stem cell was recently identified, the multipotent adult progenitor cell (MAPC) or mesodermal progenitor cell, which co-purifies with MSCs. These MAPCs differentiate into MSCs, endothelial, epithelial and even hematopoietic cells. BM stroma cells, including the primitive pluripotent MSCs and MAPCs, are attractive targets for cell and gene therapy. The BM stromal cell population and its

multipotent stem cells can be engineered to secrete a series of different
proteins in vitro and in vivo that could potentially treat a variety of
serum protein deficiencies and other genetic or acquired diseases,
including bone, cartilage and BM stromal disorders or even cancer.
RE.CNT 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 17 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
reserved on STN
AN 1997141519 EMBASE
TI Two-component signal transducers and MAPK cascades.
AU Wurgler-Murphy, Susannah M. (correspondence); Saito, Haruo
CS Division of Tumor Immunology, Dana-Farber Cancer Institute, Harvard
Medical School, Boston, MA 02115, United States.
haruo_saito@dfci.harvard.
edu
AU Wurgler-Murphy, Susannah M. (correspondence)
CS Division Tumor Immunology, Dana-Farber Cancer Institute, Boston, MA 02115,
United States.
SO Trends in Biochemical Sciences, (May 1997) Vol. 22, No. 5, pp. 172-176.
Refs: 38
ISSN: 0968-0004 CODEN: TBSCDB
PUI S 0968-0004(97)01036-0
CY United Kingdom
DT Journal; General Review; (Review)
FS 029 Clinical and Experimental Biochemistry
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 29 May 1997
Last Updated on STN: 29 May 1997
AB Two-component signal transducers, which are characterized by the
histidine-to-aspartate phospho-transfer mechanism, were once thought to be
restricted to prokaryotes. They have, however, now been identified in
diverse eukaryotic species including plant, fungus, yeast and slime mold,
In yeast, a two-component osmosensor has been found to regulate a
mitogen-activated protein kinase (MAPC) cascade, a ubiquitous
eukaryotic signaling module.

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=> FIL STNGUIDE
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         83.43      83.65

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                         -8.20
-8.20

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LAST RELOADED: Apr 17, 2009 (20090417/UP).

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     (FILE 'HOME' ENTERED AT 14:59:11 ON 20 APR 2009)

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:59:20 ON 20 APR 2009
L1           348 S MULTIPOTENT ADULT STEM CELL OR MAPC
L2             3 S L1 AND HOMOLOGOUS RECOMBIN?
L3             2 DUP REM L2 (1 DUPLICATE REMOVED)
L4            24 S L1 AND REVIEW
L5            17 DUP REM L4 (7 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:04:20 ON 20 APR 2009

=> s l1 and pY,=2002
'2002' NOT A VALID FIELD CODE
             0 MULTIPOTENT
             0 ADULT
             0 STEM
            15 CELL
             0 MULTIPOTENT ADULT STEM CELL
                 (MULTIPOTENT(W)ADULT(W)STEM(W)CELL)
             1 MAPC
             0 PY,=2002
L6           0 L1 AND PY,=2002

=> FIL BIOSIS CAPLUS EMBASE
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                          0.63      84.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)              SINCE FILE      TOTAL
                                                           ENTRY    SESSION
CA SUBSCRIBER PRICE                                          0.00
-8.20
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=> s l1 and pY<=2002
L7         135 L1 AND PY<=2002

=> dup rem l7
PROCESSING COMPLETED FOR L7
L8          88 DUP REM L7 (47 DUPLICATES REMOVED)

=> s l8 and vector
L9           0 L8 AND VECTOR

=> s l8 and recombin?
L10          0 L8 AND RECOMBIN?

=> d bib abs l8 1-10

L8   ANSWER 1 OF 88  BIOSIS  COPYRIGHT (c) 2009 The Thomson
Corporation  on STN
     DUPLICATE 1
AN   2002:496942  BIOSIS
DN   PREV200200496942
TI   Multipotent progenitor cells can be isolated from postnatal
murine bone
     marrow, muscle, and brain.
AU   Jiang, Yuehua; Vaessen, Ben; Lenvik, Todd; Blackstad, Mark;
Reyes,
     Morayma; Verfaillie, Catherine M. [Reprint author]
CS   Department of Medicine, University of Minnesota, 422 Delaware
Street SE,
     MMC 716, Minneapolis, MN, 55455, USA
     verfa001@umn.edu
SO   Experimental Hematology (Charlottesville), (August, 2002) Vol.
     30, No. 8, pp. 896-904. print.
     CODEN: EXHMA6. ISSN: 0301-472X.
DT   Article
LA   English
ED   Entered STN: 18 Sep 2002
     Last Updated on STN: 18 Sep 2002
AB   Objective: Recent studies have shown that cells from bone marrow
(BM),
     muscle, and brain may have greater plasticity than previously
known.  We
```

have identified multipotent adult progenitor cells (MAPC) in postnatal human and rodent BM that copurify with mesenchymal stem cells (MSC). BM MAPC proliferate without senescence and differentiate into mesodermal, neuroectodermal, and endodermal cell types. We hypothesized that cells with characteristics similar to BM MAPC can be selected and cultured from tissues other than BM. Materials and Methods: BM, whole brain, and whole muscle tissue was obtained from mice. Cells were plated on Dulbecco modified Eagle medium supplemented with 2% fetal calf serum and 10 ng/mL epidermal growth factor (EGF), 10 ng/mL platelet-derived growth factor (PDGF-BB), and 1000 units/mL leukemia inhibitory factor (LIF) for more than 6 months. Cells were maintained between 0.5 and 1.5X103 cells/cm2. At variable time points, we tested cell phenotype by FACS and evaluated their differentiation into endothelial cells, neuroectodermal cells, and endodermal cells in vitro. We also compared the expressed gene profile in BM, muscle, and brain MAPC by Affimetrix gene array analysis. Results: Cells could be cultured from BM, muscle, and brain that proliferated for more than 70 population doublings (PDs) and were negative for CD44, CD45, major histocompatibility complex class I and II, and c-kit. Cells from the three tissues differentiated to cells with morphologic and phenotypic characteristics of endothelium, neurons, glia, and hepatocytes. The expressed gene profile of cells derived from the three tissues was identical (r2>0.975). Conclusions: This study shows that cells with MAPC characteristics can be isolated not only from BM, but also from brain and muscle tissue. Whether MAPC originally derived from BM are circulating or all organs contain stem cells with MAPC characteristics currently is being studied. Presence of MAPC in multiple tissues may help explain the "plasticity" found in multiple adult tissues.

L8 ANSWER 2 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
DUPLICATE 2

AN 2002:174753 BIOSIS
DN PREV200200174753
TI Origin of endothelial progenitors in human postnatal bone marrow.
AU Reyes, Morayma; Dudek, Arkadiusz; Jahagirdar, Balkrishna; Koodie, Lisa;
Marker, Paul H.; Verfaillie, Catherine M. [Reprint author]
CS University of Minnesota, 422 Delaware Street SE, MMC 716, Minneapolis, MN,
55455, USA
verfa001@umn.edu
SO Journal of Clinical Investigation, (February, 2002) Vol. 109, No. 3, pp. 337-346. print.
CODEN: JCINAO. ISSN: 0021-9738.
DT Article
LA English
ED Entered STN: 6 Mar 2002
Last Updated on STN: 6 Mar 2002
AB This study demonstrates that a CD34-, vascular endothelial cadherin-
(VE-cadherin-), AC133+, and fetal liver kinase+ (Flk1+) multipotent adult
progenitor cell (MAPC) that copurifies with mesenchymal stem cells from postnatal human bone marrow (BM) is a progenitor for angioblasts. In vitro, MAPCs cultured with VEGF differentiate into CD34+,
VE-cadherin+, Flk1+ cells-a phenotype that would be expected for angioblasts. They subsequently differentiate into cells that express
endothelial markers, function in vitro as mature endothelial cells, and
contribute to neoangiogenesis in vivo during tumor angiogenesis and wound
healing. This in vitro model of preangioblast-to-endothelium differentiation should prove very useful in studying commitment to the
angioblast and beyond. In vivo, MAPCs can differentiate in response to
local cues into endothelial cells that contribute to neoangiogenesis in
tumors. Because MAPCs can be expanded in culture without obvious senescence for more than 80 population doublings, they may be an important
source of endothelial cells for cellular pro- or anti-angiogenic therapies.

L8 ANSWER 3 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:109123 CAPLUS
DN 136:291972
TI Putting the neo into neoangiogenesis
AU Moore, Malcolm A. S.
CS Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA

SO Journal of Clinical Investigation (2002), 109(3), 313-315
CODEN: JCINAO; ISSN: 0021-9738
PB American Society for Clinical Investigation
DT Journal; General Review
LA English
AB A review. The research of Reyes, M.; et al. (2002) on the participation
of endothelial cells in new blood vessel formation in normal and pathol.
states, including tumor neoangiogenesis, is reviewed with commentary and
refs. A unique cell in human and rodent postnatal marrow, designated the
multipotent adult progenitor cell (MAPC), was identified. MAPCs
were selected by depleting adult bone marrow of hematopoietic cells
expressing CD45 and glycophorin-A, followed by long-term culture of
fibronectin with EGF and PDGF under low serum conditions. The potential
of human MAPCs , obtained after 20-65 PD, to form functional endothelium,
was evaluated. The results showed that the cells form vascular tubes when
plated on Matrigel and upregulate angiogenic receptors and VEGF in
response to hypoxia. A comparison of MAPC with embryonic stem
cells and cells generated by therapeutic cloning is presented.
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:396338 CAPLUS
DN 137:319820
TI Bone marrow stromal cells as targets for gene therapy
AU Van Damme, An; Vanden Driessche, Thierry; Collen, Desire; Chuah, Marinee
K. L.
CS Center for Transgene Technology and Gene Therapy, Flanders Interuniversity
Institute for Biotechnology-University of Leuven, Louvain, B-3000, Belg.
SO Current Gene Therapy (2002), 2(2), 195-209
CODEN: CGTUAH; ISSN: 1566-5232
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
AB A review. The bone marrow (BM) is composed of the non-adherent
hematopoietic and adherent stromal cell compartment. This adherent BM
stromal cell fraction contains pluripotent mesenchymal stem cells (MSCs)

and differentiated mesenchymal BM stromal cells. The MSCs self-renew by
proliferation while maintaining their stem-cell phenotype and give rise to
the differentiated stromal cells which belong to the osteogenic,
chondrogenic, adipogenic, myogenic and fibroblastic lineages. A more
primitive adherent stem cell was recently identified, the multipotent
adult progenitor cell (MAPC) or mesodermal progenitor cell,
which co-purifies with MSCs. These MAPCs differentiate into MSCs,
endothelial, epithelial and even hematopoietic cells. BM stroma cells,
including the primitive pluripotent MSCs and MAPCs, are attractive targets
for cell and gene therapy. The BM stromal cell population and its
multipotent stem cells can be engineered to secrete a series of different
proteins in vitro and in vivo that could potentially treat a variety of
serum protein deficiencies and other genetic or acquired diseases,
including bone, cartilage and BM stromal disorders or even cancer.
RE.CNT 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2002:400175 BIOSIS
DN PREV200200400175
TI Ex vivo and in vivo primitive and definitive hematopoiesis from a
non-hematopoietic stem cell.
AU Reyes, M.; Verfaillie, C.; Koodie, L.; Lund, T.; Lenvik, T.; Jahagirdar,
B.
SO Experimental Hematology (Charlottesville), (June, 2002) Vol. 30,
No. 6 Supplement 1, pp. 42. print.
Meeting Info.: 31st Annual Meeting of the International Society for
Experimental Hematology. Montreal, Quebec, Canada. July 05-09, 2002.
CODEN: EXHMA6. ISSN: 0301-472X.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 24 Jul 2002
Last Updated on STN: 29 Aug 2002

L8 ANSWER 6 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN

AN 2003:283255 BIOSIS
DN PREV200300283255
TI HUMAN AND RAT DERIVED MULTIPOTENT ADULT PROGENITOR CELLS (MAPC) SURVIVE AND EXPRESS NEURAL MARKERS WHEN TRANSPLANTED INTO NEONATAL RATS.
AU Ortiz-Gonzalez, X. R. [Reprint Author]; Keene, C. D. [Reprint Author];
Reyes, M. [Reprint Author]; Nan, Z. H. [Reprint Author]; Duan, W. M.
[Reprint Author]; Verfaillie, C. M. [Reprint Author]; Low, W. C. [Reprint
Author]
CS Neurosurgery, Medicine, Graduate Program in Neuroscience, Stem Cell
Institute, University of Minnesota, Minneapolis, MN, USA
SO Society for Neuroscience Abstract Viewer and Itinerary Planner, (2002) Vol. 2002, pp. Abstract No. 237.19.
http://sfn.scholarone.com. cd-rom.
Meeting Info.: 32nd Annual Meeting of the Society for Neuroscience.
Orlando, Florida, USA. November 02-07, 2002. Society for Neuroscience.
DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 19 Jun 2003
Last Updated on STN: 19 Jun 2003
AB Multipotent Adult Progenitor Cells (MAPCs) have been shown to generate
tissue derivatives from each of the three embryonic germ layers both in
vivo and in vitro.)We intend to test the potential of these bone
marrow-derived cells as a source of tissue for CNS cellular repair and
replacement therapies. In order to study the survival and differentiation
of MAPCs into the mammalian postnatal brain in vivo, we transplanted
undifferentiated rat or human MAPCs intracerebroventricularly in neonatal
(P1-P3) rats. Animals were sacrificed at 2, 4 or 12 weeks of age, and
immunofluorescent studies were performed to evaluate expression of neural
markers in vivo by donor-derived cells. Human MAPCs were found in the
hippocampal formation and periventricular areas. We were able to detect
human MAPCs-derived cells that were double labeled for the human nuclear
membrane antigen and GFAP or NeuN (markers for astrocytes and neurons,

respectively). Rat MAPC-derived cells showed better survival and neural differentiation, both immunohistochemically and morphologically. eGFP+ rat MAPC-derived cells expressing NeuN or GFAP were also found, predominantly within the hippocampal formation.

These preliminary studies support the potential of MAPCs for the development of neural transplantation therapies.

L8 ANSWER 7 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2003:336702 BIOSIS
DN PREV200300336702
TI Neuralization of Hematopoietic Stem Cells; Neuroshperes Derived from Human
Umbilical Cord Blood.
AU Reems, Jo Anna [Reprint Author]; Hagman, Derek K. [Reprint Author];
Lingohr, Melissa K. [Reprint Author]; Rhodes, Christopher J. [Reprint
Author]
CS Puget Sound Blood Center/Northwest Tissue Center, Seattle, WA, USA
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2004. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology.
Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB Observations of stem cell plasticity have increasingly been reported for a
wide range of embryonic, neonatal and adult tissues. In our own investigation, ex vivo culture of the light-density fraction of nucleated
cells isolated from human umbilical cord blood was carried out in two
stages, which repeatedly produced an adherent cell population that
exhibited neural morphology. Initially, these cells were maintained in a
serum-enriched media for up to 72 hours. Following this, the cells were
sub-cultured at densities of 0.6-1.0x106 cells/ml in a serum-free
neuralization media supplemented with basic fibroblastic growth factor
(bFGF) and B27 for seven days. As a control, cord blood cells were also

sub-cultured in Myelocult H5100 or left in the serum-enriched media following the 72-hour incubation. Cell densities at 1.0x106 failed to produce an expanding adherent cell population. Neuralization of the adherent layer of cells occurred in the presence of bFGF+B27 and was confirmed via RT-PCR for the expression of the glial fibrillary acidic protein (GFAP) marker for astrocytes and microtubule-associated protein-2 (MAP2) for neurons. Fluorescent activated cell sorting (FACS) and subsequent culturing assays indicated that the neuralized cell population was derived from the CD34- cell fraction. Cord blood cells sub-cultured in Myelocult H5100 or left in the serum-enriched media following the 72-hour incubation period failed to generate neuralized cells. However, cells left in the serum-based media did produce an expanding, passage-able adherent layer characteristic of the mesenchymal stem cell (MSC) population. Two distinct types of cells, both fibroid-like and osteoclast-like cells were observed. Interestingly, exposure of the MSC-like adherent cells to the neuralization media did produce a small number of neural-like cells. However, FACS of the MSC-like cells using the CD105 and CD51/61 markers failed to produce neuralized cells. It remains to be determined if the recently described multipotent adult progenitor cells (MAPC) that co-purify with the MSC population represent the source of these neuralizing cells in hematopoietic tissues.

Finally, cord blood cultures extended out to 12 days, exhibited an abundance of cells clustered into balls, freely suspended in the media above the adherent layer. When transferred to new culture flasks containing neuralization media, these clusters typically adhere rapidly and reconstitute a new neuralized adherent layer. In one instance, however, the cell clusters produced were maintained in suspension, and using confocal microscopy stained positively for the neural markers

neurogenin-3 (Ngn3) and nestin, and for the proliferation marker Ki-67.
Presumed to be neurospheres containing neuro/epithelial progenitors, these
clusters exhibited spontaneous differentiation into structures exhibiting
astrocyte morphology and positive staining for GFAP/Ngn3 and insulin
receptor substrate-2 (IRS2). Together these results indicate that stem
cells contained within umbilical cord blood have the potential to
differentiate into cells that express markers of neural development.

L8 ANSWER 8 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2003:337290 BIOSIS
DN PREV200300337290
TI Purification of MSC from Mouse Compact Bone.
AU Short, Brenton J. [Reprint Author]; Brouard, Nathalie [Reprint Author];
Simmons, Paul J. [Reprint Author]
CS Stem Cell Biology Laboratory, Peter MacCallum Cancer Institute, East
Melbourne, VIC, Australia
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 225. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology.
Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB Adult mammalian bone marrow (BM) contains at least two distinct
populations of stem cells; those of the hematopoietic lineage and a second
population termed mesenchymal (MSC) or marrow stromal stem cells
(fibroblast colony-forming cells; CFU-F) which represent stem cells for
non-haemopoietic tissues within the BM. The progeny of these cells play a
key role in skeletal homeostasis as well as providing functional support
for the proliferation and differentiation of hematopoietic cells. Recent
studies have suggested that cells co-purifying with MSC may be multipotent
adult precursor cells (MAPC) capable of generating cells of all

three germ layers and subsequently all somatic cell types. MSC have been implicated as targets in a variety of cellular therapies for the treatment of defects of the haemopoietic and skeletal systems and as vehicles for gene therapies. Much of our understanding of the biology of these cells is based upon in vitro studies of culture selected and expanded cells. In contrast little is known about the cellular and molecular characteristics of MSC in vivo. In the mouse, major barriers to the study of MSC include their low incidence within the BM and the lack of phenotypic markers to facilitate their identification and isolation. We now describe a robust methodology for the prospective isolation of MSC in adult murine BM. In accord with previous studies, the incidence of CFU-F in mouse compact bone (CB) was significantly higher than that in BM (2689+58 vs. 102+80 colonies/106 cells respectively, n=5). Approximately 75% of total femoral CFU-F were recovered in the CB fraction. Based on these data we developed a methodology for the purification of CFU-F from mouse CB based on sequential negative selection using a panel of antibodies to cell surface molecules on mature haemopoietic lineages (Lin-) followed by positive selection using fluorescence-activated cell sorting (FACS). The CB lin- fraction, representing 5.2+ 0.5 % of the input population (n=28) exhibited a colony-forming efficiency (CFE) of 23+2.6 colonies/103 cells plated (n=4). Dual colour FACS of the Lin- CB fraction stained with antibodies to CD45 and Sca-1 resolved a discrete subpopulation of Sca-1brightCD45-Lin- cells with a CFE by limit-dilution analysis of 11.3+2%. Analysis of clones derived from single Sca-1brightCD45-Lin- cells indicate that these MSC cells have high although variable proliferative potential (50-125 population doublings) whilst maintaining at least a tripotential differentiative capacity as assessed by in vitro adipogenic, chondrogenic and osteogenic differentiation assays. Neither

freshly isolated nor cultured MSC contributed to the haemopoietic lineage following transplant into ablated recipients. Depletion of CD31+ cells from the Sca-1brightCD45- fraction increased the CFE to approximately 1 per 3 cells plated, with all assayable CFU-F recovered in the CD31- fraction. While this is by far the most highly enriched population of murine CFU-F yet described, current studies exploiting further phenotypic heterogeneity within this Sca-1brightCD45-Lin-CD31- population will likely yield a homogeneous population of MSC. These studies represent the first description of a phenotype containing a highly enriched population of mouse MSC and provide an important prerequisite not only for fundamental studies of the cellular and molecular biology of these poorly characterised stem cells but also for the development of a mouse model to investigate the utility of BM derived MSC in a range of cellular therapies.

L8 ANSWER 9 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2003:367607 BIOSIS
DN PREV200300367607
TI Transdifferentiation of Human Haemopoietic Lineage Negative Bone Marrow Cells to Neural Cells by Cytokines and Chemical Inducing Agents.
AU Tao, Helen [Reprint Author]; Rao, Renuka S. [Reprint Author]; Ma, David D. F. [Reprint Author]
CS Department of Haematology and Haematopoietic Stem Cell Transplantation, St Vincent's Hospital, Sydney, NSW, Australia
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 4123. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003

AB Adult stem cell plasticity is currently the subject of intensive research,
as it holds immense potentials for treatment of various human diseases.
several groups have demonstrated the presence of a type of stem cells in
the adult human bone marrow termed mesenchymal stem cells (MSCs)
multipotent adult progenitor cells (MAPC), capable of
differentiating into cells of ectoderm, mesoderm and endoderm origins.
interestingly these cells have the potential to differentiate into
neuronal like cells in vitro thus raising the possibility of stem cell
therapy for neural degenerative disorders such as stroke and Parkinson's
disease. Alhough a variety of reagents have been reported for inducing
neuronal differentiation, the most effective agent(s) for inducing this
lineage switch and the optimal culture conditions for long term
maintenance remain to be defined. in this study we have induced neuronal
differentiation of haemopoietic lineage negative BM cells using a cocktail
of growth factors including bFGF, EGF and PDGF. The efficiency of
neuronal induction and its maintenance in culture are compared to the
previously reported method of induction using butylated hydroxyanisole
(BHA) and dimethylsulfoxide (DMSO). BM samples from individuals collected
after consent, were subjected to gradient centrifugation followed by
plastic adherence or immunomagnetic bead sorting to obtain
cd34-/14-/45-/glycophorin-A- cells. These cells were grown in DMEM based
culture medium supplemented with or without fetal calf serum. After
several passages cells were induced with either BHA/DMSO or the cocktail
of growth factors. Morphologically, induction with BHA/DMSO resulted in a
uniform neuronal-like cell population within 6 hrs. Also expression of
neuronal specific markers and genes such as NSE, NeuN, NF-M, MAP2, b
tubulin III and tau could be detected. However these cells could not be
maintained in culture for more than 7 days. In contrast the cells induced

with the combination of growth factors showed a gradual change in morphology over a period of few weeks but were more stable and have been maintained in culture for 2-3 months without loss of neuronal properties. The growth factors induced differentiation, also produced a heterogeneous population of neural cells which included neurons, astrocytes and oligodendrocytes based on the expression of neural specific markers (genes and proteins) and also neurotransmitters such as dopamine, g-aminobutyric acid and serotonin. This study demonstrates that growth factors can induce stable populations of neural cells. further, preliminary work has raised the possibility of obtaining homogeneous subpopulations of neural cells by using different combinations of these growth factors thereby providing cell populations suitable for therapeutic use in a variety of neurodegenerative diseases. Work is in progress to optimize this transdifferentiation process and also to elucidate the underlying mechanism.

L8 ANSWER 10 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2003:336751 BIOSIS
DN PREV200300336751
TI Heparan Sulfate Oligosaccharides Modulate the Proliferation and Differentiation of Human Multipotent Progenitor Cells.
AU Gupta, Pankaj [Reprint Author]; Pan, Chendong [Reprint Author]; Nelson, Matthew S. [Reprint Author]; Reyes, Morayma [Reprint Author]
CS Hem/Onc Section, VA Med. Ctr., Minneapolis, MN, USA
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2054. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology. Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB Cell surface and matrix (ECM) heparan sulfate (HS) influences embryogenesis by binding to and modulating the activity of several

cytokines (CK). The biological activity of FGF-2, critical for neurogenesis and angiogenesis, requires the formation of a signaling complex of FGF-2, FGF receptor (FGFR) and cell surface HS (FGF-FGFR-HS).

Our group has shown that specific CK induce in vitro differentiation of multipotent adult progenitor cells (MAPC) into mesodermal, endodermal and neuro-ectodermal lineages (Reyes M. Blood 98:2615, 2001; Jiang Y. Nature 418:41, 2002). When cultured with FGF-2, MAPC acquire a neuronal and glial phenotype. MAPC thus provide a powerful model for studying the effect of ECM components like HS, on CK signaling and stem cell growth and differentiation. We used this model to examine if and how FGF-2-HS interactions influence MAPC proliferation and neuronal differentiation. Further, to determine if and how abnormal HS perturb stem cell proliferation and differentiation, we compared MAPC from patients with Hurler syndrome, an inborn metabolic error with accumulation of structurally abnormal HS and progressive neurological dysfunction. HS from normal MAPC bound avidly to FGF-2 (Kd 69 nM). In contrast, subpopulations of Hurler HS either bound to FGF-2 with abnormally low affinity (Kd 125 nM), or failed to bind at all. Consistent with this abnormality, the binding of 125-I-FGF-2 to Hurler MAPC (in the FGF-FGFR-HS complex) was 55% of that to normal MAPC. Hurler HS reduced the binding of 125-I-FGF-2 to normal MAPC by 50%, indicating that these abnormal HS interfere with FGF-2 binding in the FGF-FGFR-HS complex.

Enzymatic removal of Hurler cell surface HS, followed by addition of normal HS, doubled the 125-I-FGF-2 binding to Hurler MAPC. We next compared the biological effect of the interactions between FGF-2 and normal HS vs Hurler HS. FGF-2 mediated proliferation of normal MAPC required normal HS, as it was completely abrogated by enzymatic removal of cell surface HS and completely restored by addition of normal HS, but not by addition of Hurler HS. In contrast, Hurler MAPC failed to proliferate in presence of FGF-2. Further, Hurler HS markedly impaired FGF-2 mediated proliferation of normal MAPC. Enzymatic removal of the interfering cell surface HS from Hurler MAPC, followed by addition of normal HS, restored FGF-2 responsiveness. We also examined if MAPC HS induces FGF-2 signaling in HS-deficient target cells (FGFR1 transfected F32 cells that

depend on exogenous HS). FGF-2 induced proliferation of F32 cells was
significantly greater in presence of normal HS compared to Hurler HS.
Finally, while normal MAPC acquired the immunophenotype of neuronal cells, astrocytes and oligodendrocytes when cultured with FGF-2,
Hurler MAPC failed to differentiate into cells with a neuronal immunophenotype under the same conditions, and instead generated astrocytic and oligodendrocytic cells. Commitment of Hurler MAPC to the neuronal lineage (but not glial lineage) was blocked at an early
stage of differentiation, consistent with defective FGF-2 signaling
mediated by abnormal HS. These studies indicate that (i) HS is critical
for CK-mediated proliferation and differentiation of progenitor cells (ii)
in presence of the same CK, the differentiation pathway followed by a
progenitor cell may depend on the type of HS present, and most importantly, that (iii) normal HS can restore CK signaling and biological
response in progenitor cells in diseases with abnormal HS.

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FULL ESTIMATED COST	1.82	125.88

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     (FILE 'HOME' ENTERED AT 14:59:11 ON 20 APR 2009)

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:59:20 ON 20 APR 2009
L1          348 S MULTIPOTENT ADULT STEM CELL OR MAPC
L2            3 S L1 AND HOMOLOGOUS RECOMBIN?
L3            2 DUP REM L2 (1 DUPLICATE REMOVED)
L4           24 S L1 AND REVIEW
L5           17 DUP REM L4 (7 DUPLICATES REMOVED)

     FILE 'STNGUIDE' ENTERED AT 15:04:20 ON 20 APR 2009
L6            0 S L1 AND PY,=2002

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:09:37 ON 20 APR 2009
L7          135 S L1 AND PY<=2002
L8           88 DUP REM L7 (47 DUPLICATES REMOVED)
L9            0 S L8 AND VECTOR
L10           0 S L8 AND RECOMBIN?

     FILE 'STNGUIDE' ENTERED AT 15:13:42 ON 20 APR 2009

     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:29:02 ON 20 APR 2009

=> d bib abs l8 11-20

L8   ANSWER 11 OF 88  BIOSIS  COPYRIGHT (c) 2009 The Thomson
Corporation  on
     STN
AN   2003:336753  BIOSIS
DN   PREV200300336753
TI   Formation of Multinucleated Myotubes from Human Multipotent Adult
     Proenitor Cells.
AU   Muguruma, Yukari [Reprint Author]; Nakamura, Yoshihiko [Reprint
Author];
     Yahata, Takashi [Reprint Author]; Ando, Kiyoshi [Reprint
Author]; Kato,
     Shun-ich [Reprint Author]; Hotta, Tomomitsu [Reprint Author]
CS   Reserch Center for Regenerative Medicine, Tokai University
School of
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Medicine, Kanagawa, Japan
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2056. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology.
Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB Recent studies have shown that multipotent adult progenitor cells (
MAPC) derived from post-natal bone marrow can differentiate into osteoblasts, chondrocytes, adipocytes as well as endothelial cells and
hepatocyte-like cells. Several studies also reported myotubes can be
derived from bone marrow cells; however, in their system treatment with
demethylation drugs, known mutagen such as 5 azacytidine, seems to be
essential for inducing myotube formation, which hinders from therapeutic
use. We here demonstrate the derivation of multinucleated myotubes from
human adult bone marrow MAPC using clinically applicable culture condition. Frozen (n=20) and fresh (n=3) bone marrow cells were used as a
source of MAPCs. MAPCs were established according to the published method
(Blood, 2001). Briefly, fresh bone marrow cells were negatively selected
for CD45-/GryA- cells before plating, and emerging adherent cells were
expanded. On the other hand, frozen cells were plated as mononuclear
cells and cultured for 2apprx3 weeks, and then CD45-/GryA- cells were
selected. Adherent cells growing in both cultures were maintained at
500apprx3000 cells/cm2 and routinely expanded more than 25 population
doublings before using for the study. Cytogenetic analysis detected no
abnormality. To induce multinucleated myotube formation, cells were
transferred to medium containing 5% FCS, bFGF, VEGF and IGF-1, and allowed

to become confluent. Differentiation was confirmed by the expression of
myogenic markers using RT-PCR and immunocytochemical staining. A time
course analysis revealed the presence of scattered MyoD and myogenin
positive mononuclear cells by day 7. It appeared that in situ
proliferation of those cells led to the formation of myotubes. Around day
10, numerous multinucleated tubes, which were positive for alpha-actinin
and skeletal myosin, were evident. Typical striated muscle ultrastructure
was demonstrated in electron microscopy. Addition of BMP4 in the culture
appeared to facilitate cell proliferation and/or cell fusion, resulting in
the increased number of nuclei in myotubes as well as number of myotubes
formed in the culture. At day 14, mononuclear cells that were positive
for MyoD and myogenin remained in the culture, indicative of heterogeneity
in cell maturation in our culture system and continuous new myotube
formation. All in all, we have successfully induced multinucleated
myotubes from adult bone marrow MAPC in vitro, which will be
useful in treatment or improvement of life quality in patients with
musclular disorders. To assess the engraftment and differentiation of
MAPC derived muscle cells in vivo, eGFP-transduced MAPC
with or without myogenic induction were injected into tibialis anterior
muscles of NOD/SCID mice. The result of in vivo study is currently under
analysis.

L8 ANSWER 12 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2003:336377 BIOSIS
DN PREV200300336377
TI Ex Vivo Differentiation of Mouse Multipotent Adult Progenitor Cells
(mMAPC) into Functional Dopaminergic Neurons.
AU Jiang, Yuehua [Reprint Author]; Henderson, Dori [Reprint Author];
Blackstedt, Mark [Reprint Author]; Chen, Angel [Reprint Author]; Lisberg,
Aaron [Reprint Author]; Miller, Robert F. [Reprint Author]; Verfaillie,

Catherine M. [Reprint Author]
CS Stem Cell Institute and Department of Medicine, University of Minnesota,
Minneapolis, MN, USA
SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 95. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology.
Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB Recently we reported that a rare cell, termed Multipotent Adult Progenitor
Cells or MAPC, within mouse bone marrow mesenchymal stem cell
cultures can be expanded without obvious senescence, differentiate in
vitro to cells of the three germ layers, and contribute to most somatic
tissues when injected into an early blastocyst. Here we demonstrate that
mMAPC can differentiate to functional dopaminergic neurons in vitro.
MAPC were cultured in FN-coated wells in serum-free medium without
EGF, PDGF, LIF (cytokines required for maintenance of MAPC)
sequentially for 7 days with 100ng/ml bFGF in serum-free medium, followed
by 7 days with 10ng/ml FGF-8 plus 100ng/ml Sonic Hedgehog (SHH), followed
by 10 ng/ml BDNF in N2 medium. On day 21, MAPC-progeny was
co-cultured with murine fetal astrocytes in N2 medium for an additional 7
days. Quantitative RT-PCR was used to detect expression of
neuroectodermal genes. Levels of Otx2 mRNA increased more than 50-fold by
day 2 and became maximal by day5. On day 4, Otx1 mRNA was upregulated 3
to 5-fold, and on day 5 levels of Pax2, Pax5 and nestin mRNA increased 400
to 800-fold over undifferentiated MAPC. On day 11 levels of
Nurr1 increased 600-fold over undifferentiated mMAPC and TH mRNA was
detectable. On day 14, cells staining positive for glial fibrillary
acidic protein (GFAP/astrocytes; 25%), myelin basic protein
(MBP/oligodendrocytes; 25%) and neurofilament-200 (NF200 neurons; 50%)

could be detected. On day 21, neurons acquired a more mature phenotype,
demonstrating polarization, and expression of neurotransmittors (GABA,
dopamine and serotonin). However, electrophysiological studies did not
demonstrate presence of voltage-gated sodium-channels. After 28 days of
sequential treatment of cytokines and co-culture with astrocytes, neurons
matured further. Immunoflurescence microscopy showed that 20-30% of cells
were dopadecarboxylase (DDC) and tyrosine hydroxylase (TH) positive,
20-30% trytophan hydroxylase (TrH) positive and 50-60% GABA positive. 14
mature-neuron-like cells were chosen for patch clamp evaluation of current
and voltage clamp recordings. In 10/14 cells sodium currents and spiking
could be evoked. Of them current injection evoked repetitive spiking in 4
of the cells and single spiking in 6 cells. Voltage-clamp recordings from
the spiking cells demonstrated the presence of tetrodotoxin-sensitive
inward currents, indicating that currents were mediated by voltage-gated
sodium channels. These data demonstrated therefore that MAPC can differentiate in vitro to functional dopaminergic neurons. As
MAPC can be purified and expanded from marrow, they may constitute
a useful source to treat Parkinson disease. In vivo study is currently
going on.

L8 ANSWER 13 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2003:337272 BIOSIS
DN PREV200300337272
TI Efficient Transfection of Human CD34+ Cells with "Sleeping Beauty" DS-RED
Transposons.
AU Lamming, Christopher E. [Reprint Author]; Converse, Andrea [Reprint
Author]; Augustine, Lance [Reprint Author]; McIvor, R. Scott [Reprint
Author]; Verfaillie, Catherine M. [Reprint Author]
CS Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA

SO Blood, (November 16 2002) Vol. 100, No. 11, pp. Abstract No. 2574. print.
Meeting Info.: 44th Annual Meeting of the American Society of Hematology.
Philadelphia, PA, USA. December 06-10, 2002. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003
AB The promise of hematopoietic stem cell (HSC) gene therapy has been limited by low viral transduction efficiencies of HSC and potential dangers of using viral agents in a clinical setting. Non-viral gene therapy is a safer alternative to viral based systems. The transposon plasmid based system has been successfully used to stably introduce non-viral DNA into hematopoietic cell lines. However, CD34+ stem cells remain difficult to target as shown by NOD-SCID repopulation assays of transfected cells (Hossle J.P., 2002). We tested whether CD34+ cells could be stably transfected with DS-RED expressing transposons. DS-RED plasmids were constructed with or without transposase with CMV or CAGGS promoters driving DS-RED expression. Plasmid size was 11-15 Kb, depending on the presence of transposase. 60mug/mL plasmid DNA was either electroporated or nucleoporated. Electroporation conditions were: 250v, 1600muF in a 0.5ml cuvette. Nucleoporation conditions were CD34+ nucleoporation media and machine setting U08. 2x105-2x106 cord blood CD34+ cells were electroporated in media containing X-VIVO 10, 5% FCS, 20 ng/ml SCF, Flt-3L, IL7 and TEPO at 250v, 1600muF. After nucleoporation or electroporation, cells were pelleted and incubated at 37degreeC for 15min before transfer to transwells over AFT024 stroma in media containing RPMI1640, 20% FCS and cytokines as above. 72 hours later, cells were harvested, stained with Annexin V and 7AAD, and live DS-RED positive cells

selected by FACS. 20-40% of electroporated and 10-35% of nucleoporated
CD34+ samples were DS-RED positive. However, Annexin V and 7AAD staining
showed that most transfected cells were undergoing apoptosis. Only
2.5+-0.3% of electroporated and 2%+-0.6% of nucleoporated CD34+ cells were
Annexin V-7AAD-DS-RED+, which were then deposited on AFT024 feeders at 10
cells/well. Wells were scored 1, 2 and 3 weeks later for DS-RED+ cells.
After 1 week, 80+-5% of electroporated or nucleoporated CD34+ progeny were
positive, and after 2 and 3 weeks, 67+-6% were DS-RED positive.
Confirmation of DNA integration using PCR is underway. Likewise, studies
are underway to demonstrate that CD34+ cells still retain CFC activity.
We are also investigating the possibility of using this method to
introduce DS-RED plasmids into a rare population of stem cells, recently
identified in our laboratory in human and rodent marrow, termed
multi-potent adult progenitor cells, or MAPC, that may be an
attractive alternative for gene therapy as they can contribute up to 10%
of the hematopoietic system following transplantation into a minimally
irradiated recipient. We have shown higher rates of transfection
(4.8+-0.6%) and long term expression of DS-RED in MAPC by
fluorescence(78+-8% at 4 weeks) but have not yet shown definitive
differentiation ability of DS-RED expressing progeny to mesodermal,
endodermal and ectodermal lineages. In conclusion although low rates of
transfection are seen, Transposon-based non-viral vectors hold promise for
hematopoietic stem cell gene therapy. In addition MAPC, that
can likewise be transfected with the Transposon system, may prove to be an
attractive target for clinical transplantation due to the ability to
expand transfected MAPC long-term without loss of engraftment
and multi-lineage differentiation ability.

AN 2002201327 EMBASE
TI Embryonic stem cell research: The relevance of ethics in the progress of
science.

AU Ruiz-Canela, Miguel (correspondence)
CS Department of Biomedical Humanities, University of Navarra, Apartado 177,
E-31080 Pamplona, Spain. mcanela@unav.es
SO Medical Science Monitor, (2002) Vol. 8, No. 5, pp. SR21-SR26.
Refs: 50
ISSN: 1234-1010 CODEN: MSMOFR
CY Poland
DT Journal; Article
FS 017 Public Health, Social Medicine and Epidemiology
029 Clinical and Experimental Biochemistry
LA English
SL English
ED Entered STN: 27 Jun 2002
Last Updated on STN: 27 Jun 2002
AB Experimentation with embryonic stem (ES) cells has become an important
breakthrough in medical research. However, it is also a source of
controversy, because it requires the destruction of the human embryos used
to derive ES cells. This paper deals with some of the ethical issues
concerning ES cell research. To begin with, the terms used in the debate
on the ethical status of the human embryo need to be defined. Apart from
the presumed benefits of ES cell research, we should also consider such
issues as the strong opposition to this research by a large part of
society, who argue in favour of protecting and respecting human embryos;
the fragility and defenseless of human embryos; and the contradiction in
terms inherent in the statement that human embryos must be treated with
respect. Secondly, we should focus on possible conflicts between the
financial, scientific, and ethical aspects of this debate. Thirdly, the
significance of social and political debate requires clear and complete
information that takes all consequences into account. Finally, the paper
suggests how multipotent adult stem
cell research may be an optimal and realistic alternative to ES
cell research.

L8 ANSWER 15 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2002:642936 CAPLUS
DN 137:349940

TI Purification, characterization and differentiation of multipotent adult stem cell from post-natal human bone marrow
AU Reyes, Morayma Gil
CS Univ. of Minnesota, Minneapolis, MN, USA
SO (2001) 202 pp. Avail.: UMI, Order No. DA3029106
From: Diss. Abstr. Int., B 2002, 62(10), 4322
DT Dissertation
LA English
AB Unavailable

L8 ANSWER 16 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2001:115268 CAPLUS
DN 134:159887
TI Multipotent adult stem cells and methods for isolation
IN Furcht, Leo T.; Verfaillie, Catherine M.; Reyes, Morayma
PA USA
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001011011	A2	20010215	WO 2000-US21387	20000804 <--
WO 2001011011	A3	20010510		
WO 2001011011	A9	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2381292	A1	20010215	CA 2000-2381292	20000804 <--
AU 2000066218	A	20010305	AU 2000-66218	20000804 <--
AU 784163	B2	20060216		
EP 1226233	A2	20020731	EP 2000-953840	20000804 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL

	JP 2003506075	T	20030218	JP 2001-515800 20000804
	NZ 517002	A	20040625	NZ 2000-517002 20000804
	ZA 2002001125	A	20040510	ZA 2002-1125 20020208
	IN 2002CN00311	A	20070223	IN 2002-CN311 20020228
	US 20050181502	A1	20050818	US 2005-84256 20050321
	US 20060008450	A1	20060112	US 2005-151689 20050613
	US 20060030041	A1	20060209	US 2005-238234 20050929
	US 20060263337	A1	20061123	US 2005-269736 20051109
	AU 2006202072	A1	20060615	AU 2006-202072 20060516
	US 20070009500	A1	20070111	US 2006-446560 20060602
	JP 2008044965	A	20080228	JP 2007-273194 20071019
	IN 2008CN02360	A	20090306	IN 2008-CN2360 20080512
PRAI	US 1999-147324P	P	19990805	
	US 1999-164650P	P	19991110	
	AU 2000-66218	A	20000804	
	JP 2001-515800	A3	20000804	
	WO 2000-US21387	W	20000804	
	US 2001-268786P	P	20010214	
	US 2001-269062P	P	20010215	
	US 2001-310625P	P	20010807	
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	WO 2002-US4652	W	20020214	
	IN 2002-CN311	A3	20020228	
	US 2002-48757	A1	20020821	
	US 2003-527249P	P	20031204	
	US 2004-467963	A2	20040105	
	US 2004-963444	B2	20041011	
	WO 2004-US40932	A1	20041206	
	US 2005-84256	A2	20050321	
	US 2005-151689	A2	20050613	

AB The invention provides isolated stem cells of non-embryonic origin that can be maintained in culture in the undifferentiated state or differentiated to form cells of multiple tissue types. Also provided are methods of isolation and culture, as well as therapeutic uses for the

isolated cells. Multipotent adult stem cells were obtained from bone
marrow mononuclear cells of humans and mice by depletion of CD45-pos. and
glycophorin A-pos. cells with microbeads. Conditions are described for
culturing the cells and for differentiating them into many kinds of cells.
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2001:68346 CAPLUS
TI Method of reducing turbo lag in diesel engines having exhaust gas recirculation
IN Kolmanovsky, Ilya V.; Van Nieuwstadt, Michiel J.; Moraal, Paul Eduard
PA Ford Motor Company, USA
SO U.S., 10 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6178749	B1	20010130	US 1999-237737	19990126 <--

PRAI US 1999-237737 19990126
AB A method of reducing turbo lag in a compression ignition engine having an
exhaust gas recirculation system (EGR) and a variable geometry
turbocharger (VGT). The method includes the steps of determining an intake
manifold pressure and intake manifold mass airflow setpoint, MAPd and
MAFd, as a function of the current engine speed and requested fueling rate
(Wf,REQ). The method further includes modifying the setpoints by a
transient governor to generate modified setpoints, MAFc and MAPc
, as a function of MAFd and MAPd, resp., and feeding the modified
setpoints to the controller to drive the turbocharger and EGR valve to the
desired setpoints, thereby maximizing the amount of fresh air admitted to
the engine during transient operation. Another embodiment of the method
for reducing turbo lag coordinates the controller gains between the EGR
and VGT. The method speeds up the MAF response by using multivariable

control of both the EGR and VGT to aggressively regulate airflow to the
desired setpoint.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2002:261590 BIOSIS
DN PREV200200261590
TI Microarray analysis of differentiation from MAPC to osteoblasts.
AU Qi, Huilin [Reprint author]; Aguiar, Dean [Reprint author]; Verfaillie,
Catherine [Reprint author]
CS Medicine, Stem Cell Institute, University of Minnesota, Minneapolis, MN,
USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 832a.
print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 1 May 2002
Last Updated on STN: 1 May 2002
AB Human bone marrow derived multipotent adult progenitor cells (MAPC
) differentiate into osteoblasts, chondrocytes, adipocytes, myocytes,
endothelial cells and neuronal cells. In order to identify genes involved
in commitment of MAPC to osteoblasts, we examined differentially
expressed genes by microarray analysis in MAPC and MAPC
treated with beta-glycerophosphate, Dexamethasone and ascorbic acid to
induce the osteoblast phenotype. Total RNA from MAPC isolated
from three donors and MAPC induced to osteoblast cell lineage at
days 1, 2 and 7 were hybridized to microarrays from Research Genetics
(4324 human genes). We found that 157 genes are up regulated (gtoreq2
fold), 212 genes are down regulated (gtoreq2 fold) in day 1 differentiated
cells. 310 genes are up and 432 are down regulated by day 2; and 787 up
and 358 down regulated by day 7. Three transcription factors were up

regulated at all three time points: DGSI, which belongs to TBX family and known to have a possible role in osteogenesis, DSIPI and BRCA-1. Some transcription factors were up regulated only on day 1, such as CLIM1, and some were only up regulated on day 2, such as AP-4, USF2, HOXA5, and HOX11. HOX11 is known to play a role in osteogenesis and chondrogenesis. The transcription factors HEMX1, Sox22, short stature homeobox 2 and cbfa3 were up regulated on both days 2 and 7, MSX2, Sox3, Sox4, MEF2b, MEF2D, NFIC and NFIX were among transcription factors up regulated on day 7. MSX2 is required for induction of CbFa1, the master transcription factor for osteoblast differentiation, which did not become up regulated until day 7 (detected by microarray analysis and Real Time RT-PCR) and 14 (detected by Real Time RT-PCR). Thirty-seven transcription factors were down regulated during differentiation, including ID3, CA150, Zinc finger proteins 6 and 162, and early growth response 1 which were suppressed at all three time points (days 1, 2, and 7) examined. CITED2 was down regulated at day 2. FUSE1 known to be more active in undifferentiated cells was down regulated at both days 2 and 7. The transcriptional repressor ZF87/MAZ, a known inhibitor of the parathyroid hormone receptor (a critical receptor in osteogenesis) gene expression, was suppressed by day 7 of MAPC differentiation to the osteoblast phenotype. Using Real Time RT-PCR we have confirmed differential expression of >20 genes as detected by microarray analysis. As up-regulation of cbfa1 was only seen after 7-14 days, microarray analysis of differentiation of MAPC to the osteoblast lineage and other lineages should provide important new insights in the pivotal molecular events required for osteoblast and other differentiation.

L8 ANSWER 19 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on

STN
AN 2002:261548 BIOSIS
DN PREV200200261548
TI Origin of endothelial progenitors in human post-natal bone marrow.
AU Reyes, Morayma [Reprint author]; Dudek, Arek; Jahagirdar, Balkrishna;
Koodie, Lisa; Verfaillie, Catherine
CS Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 821a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 1 May 2002
Last Updated on STN: 1 May 2002
AB Until recent, it was thought that blood vessel formation in post-natal
life was mediated by sprouting of endothelial cells from existing vessels.
However, recent studies have suggested that endothelial "stem cells" may
persist into adult life, where they contribute to the formation of new
blood vessels, suggesting that like during development neoangiogenesis in
the adult may at least in part depend on a process of vasculogenesis.
Precursors for endothelial cells have been isolated from BM and peripheral
blood. The ontogeny of these endothelial progenitors is unknown. We have
previously described a rare cell in human post-natal bone marrow capable
of differentiating not only in mesenchymal cell types, but also cells of
neuroectodermal origin, termed multipotent adult progenitor cell or
MAPC. We here show that these CD34-, vascular-endothelial (VE)-cadherin-, AC133+ and fetal liver kinase (Flk1)+ MAPC that co-purifies with mesenchymal stem cells is a progenitor for the angioblasts. In vitro, MAPC cultured for 3 days with vascular endothelial growth factor (VEGF) differentiated into CD34+, VE-cadherin+,
Flk1+ cells, a phenotype consistent with angioblasts. Subsequently,

MAPC differentiated into cells that express mature endothelial markers, such as vWF, Muc-18, CD36, CD31, CD62-P, Tie and Tek. In vitro generated endothelial cells from MAPC functioned as mature endothelial cells, as they (A) could uptake LDL; (B) secreted vWF and widened gap junctions under histamine exposure; (C) reacted to inflammatory cytokines (IL-1a) by upregulating HLA-Class I/II and VCAM, CD62P/E; (D) upregulated VEGF secretion and VEGFR expression under hypoxia and; (E) formed vascular tubes when plated on ECM. When infused in vivo, endothelial cells generated in vitro from MAPC contributed approximately 40% to neoangiogensis in the setting of tumor angiogenesis and wound healing. Moreover, undifferentiated MAPC infused in NOD-SCID mice differentiated in vivo in response to local cues in tumors into endothelial cells that contribute to tumor neoangiogenesis. This in vitro model of pre-angioblast to endothelium differentiation should prove very useful to study commitment to the angioblast stage and beyond. Because MAPC can be culture expanded without obvious senescence for >80 population doublings, they may be an important source of endothelial cells for cellular pro- or anti-angiogenic therapies.

L8 ANSWER 20 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2002:261451 BIOSIS
DN PREV200200261451
TI Functional abnormalities in heparan sulfate in Hurler syndrome are associated with defective differentiation of multipotent adult progenitor cells.
AU Gupta, Pankaj [Reprint author]; Reyes, Morayma; Verfaillie, Catherine M.; Nelson, Matthew S. [Reprint author]
CS Medicine/Hem-Onc, VA Med. Center, Minneapolis, MN, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 797a. print. Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 1 May 2002
Last Updated on STN: 1 May 2002
AB Hurler syndrome (mucopolysaccharidosis type I) is an inborn error of metabolism in which absence of a degradative enzyme leads to progressive tissue accumulation of heparan and dermatan sulfates (HS, DS). How these incompletely digested HS and DS cause abnormalities in the development and functioning of diverse tissues is unclear. It is known that HS directly influence normal tissue morphogenesis by binding to and modulating the activity of several proteins involved in signaling and developmental patterning. FGF-2, which plays a critical role in neuronal development, angiogenesis and hematopoiesis, is one such protein dependent on specific interactions with HS for biological activity. Thus far, the inability to obtain primary Hurler cells that are representative of cell types in diverse tissues and can be expanded easily in vitro, has been a major limitation to performing functional studies on HS in Hurler syndrome. We hypothesized that the abnormal size and sulfation of Hurler HS leads to aberrant functional properties (affinity for binding critical cytokines), which contribute to abnormalities in developing tissues (e.g., neurons). We examined the structure and function of HS purified from multipotent adult progenitor cells (MAPC) that we have identified and cultured from Hurler and normal BM. Normal MAPC can differentiate in vitro into mesodermal, endodermal and ectodermal lineages, including neuronal and glial cells. We found that the structure of HS accumulated in the extracellular matrix (ECM) of Hurler MAPC is markedly abnormal. HS molecules from Hurler cells were small (5 kD vs 42 kD), highly sulfated (65% vs 22% sulfation of total HS), and had abnormal oligosaccharide domains, compared to HS from normal MAPC . To determine if structural abnormalities identified in Hurler HS result

in abnormal function, we examined the binding of HS from the ECM of normal and Hurler MAPC to FGF-2. HS from normal MAPC bound to FGF-2 as a homogenous population (Kd 69 nM). In contrast, in Hurler HS, 3 subpopulations were identified with markedly different FGF-2 affinities: (i) the major subpopulation of Hurler HS bound with abnormally low affinity (Kd 125 nM), (ii) a second subpopulation of HS failed to bind altogether, and (iii) only the smallest (minor) subpopulation bound with normal affinity (Kd 74 nM) to FGF-2. Hurler HS also bound abnormally to SDF-1alpha and SDF-1beta, chemokines that are required for stem cell homing and migration and for cerebellar development. These data indicate that structurally abnormal HS deposited in the ECM of Hurler cells has abnormal cytokine binding properties. Finally, we examined if the abnormal interactions between Hurler HS and FGF-2 impair the biological activity of FGF-2. Whereas normal MAPC consistently differentiated into neuronal cells, astrocytes and oligodendrocytes when cultured in presence of FGF-2, Hurler MAPC failed to differentiate into neuronal cells under the same conditions, and only generated astrocytes and oligodendrocytes. Our studies thus identify for the first time a mechanism by which accumulated HS contribute to the developmental pathophysiology of Hurler syndrome (and likely other mucopolysaccharidoses), by perturbing critical HS-protein interactions.

These studies also strengthen the rationale for a therapeutic trial of normal/gene corrected MAPC, which can directly differentiate into neuronal and other cell types.

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     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 14:59:20 ON 20 APR 2009
L1           348 S MULTIPOTENT ADULT STEM CELL OR MAPC
L2             3 S L1 AND HOMOLOGOUS RECOMBIN?
L3             2 DUP REM L2 (1 DUPLICATE REMOVED)
L4            24 S L1 AND REVIEW
L5            17 DUP REM L4 (7 DUPLICATES REMOVED)

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     FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:09:37 ON 20 APR 2009
L7           135 S L1 AND PY<=2002
L8            88 DUP REM L7 (47 DUPLICATES REMOVED)
L9             0 S L8 AND VECTOR
L10            0 S L8 AND RECOMBIN?

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FILE 'STNGUIDE' ENTERED AT 15:31:51 ON 20 APR 2009

FILE 'BIOSIS, CAPLUS, EMBASE' ENTERED AT 15:36:18 ON 20 APR 2009

=> d bib abs l8 21-50

L8 ANSWER 21 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2002:261423 BIOSIS
DN PREV200200261423
TI Pluripotent nature of cells in adult marrow copurifying with mesenchymal
stem cells.
AU Jiang, Yuehua [Reprint author]; Jahagirdar, Balkrishna [Reprint author];
Largaespada, David [Reprint author]; Reyes, Moryama [Reprint author];
Lisberg, Aaron [Reprint author]; Verfaillie, Catherine M. [Reprint author]
CS Medicine and Laboratory Medicine, Stem Cell Institute, University of
Minnesota, Minneapolis, MN, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 791a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 1 May 2002
Last Updated on STN: 20 May 2002
AB A number of recent studies have suggested that adult stem cells from a
number of tissues may have greater differentiation potential than
previously thought. We have identified multipotent adult progenitor cells
or MAPC, which are co-purified with mesenchymal stem cells and
have the ability to differentiate in vitro into most mesodermal cell types
as well as cells with neuroectodermal and endodermal features (See Jiang
et al). In this study, we tested whether MAPC can differentiate
into functional cells of all tissues in vivo, by injecting them in early

blastocysts. MAPC were generated from marrow of beta-galactosidase (beta-gal) transgenic ROSA26 mice. One or 10-12 ROSA26 MAPC were microinjected into 116 and 38 early blastocysts, resp. Blastocysts were transferred to foster mothers, the mice were allowed to develop, and then 7 litters were born. The number of mice per litter varied from 1 to 8, for a total of 35 mice. Animals born from microinjected blastocysts were of similar size as normal animals and did not display any overt anatomical abnormalities. All of the mice derived from blastocysts in which 10-12 MAPC had been injected and 50% of the mice derived from blastocysts microinjected with 1 MAPC had >1% of cells in the tail that contained the NEO transgene compared to ROSA26 mice from which MAPC were derived. MAPC contributed to all tissues, including the central nervous system, skeletal muscle, cardiac muscle, liver, intestine, lung, kidney, spleen, marrow, blood, and skin as shown by X-GAL staining and staining with an anti-beta-gal-FITC antibody. beta-gal+ cells expressed markers typical for the tissue in which they incorporated. Co-labeling was seen for beta-gal, cardiac troponin-I and dystrophin in the heart, and beta-gal and skeletal actin or dystrophin in the skeletal muscle. Co-staining for beta-gal, albumin and anti-cytokeratin (CK)-18 was seen in the liver and pan-CK and beta-gal in the intestine and skin. beta-gal+ cells in the kidney co-stained with vimentin (glomeruli) or pan-CK (tubuli). Cells in spleen, bone marrow and blood showed co-labeling with anti-beta-gal and anti-CD45, anti-CD19, anti-CD3, anti-Gr1 and anti-Mac1 antibodies. In the central nervous system, we saw co-labeling of cells for beta-gal and NF200, GFAP, and MBP. As all animals had normal organs function, MAPc differentiate in vivo into functional cells of the three germ layers.

Similar results were seen for animals derived from blastocysts in which 1 or 10-12 MAPC had been injected, indicating that chimerism following blastocyst injection occurs from a single MAPC.

Together with the data presented elsewhere from our group showing that MAPC engraft and differentiate in vivo when transplanted

postnatally in uninjured animals (Jahagirdar et al), results reported here
prove the notion that adult stem cells have significantly greater differentiation potential than previously thought, and that some adult
stem cells are pluripotent.

L8 ANSWER 22 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2002:261424 BIOSIS
DN PREV200200261424
TI Multipotent adult progenitor cells from bone marrow differentiate into
urea producing hepatocyte-like cells.
AU Schwartz, Robert E. [Reprint author]; Jiang, Yuehua [Reprint author];
Blackstad, Mark [Reprint author]; Reyes, Moryama [Reprint author];
Verfaillie, Catherine M. [Reprint author]
CS Medicine, Stem Cell Institute, University of Minnesota, Minneapolis, MN,
USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 791a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 1 May 2002
Last Updated on STN: 1 May 2002
AB We have identified a population of primitive cells in normal human, mouse
and rat post natal bone marrow that we have termed Multipotent Adult
Progenitor Cell or MAPC that have multipotential differentiation
and extensive proliferation potential. MAPC differentiate in vitro into most mesodermal and neuroectodermal lineages and in vivo into
all embryological lineages (see abstracts Jiang et al). Several groups
have demonstrated that hepatocytes and cholangiocytes can be derived from
bone marrow in vivo. We investigated whether rat MAPC can differentiate into hepatocytes in vitro. MAPC were initially plated at 19,000 cells/cm2 on fibronectin coated plates and chamber slides

with 2% FCS containing medium supplemented with EGF, PDGF and LIF, medium
used to expand MAPC. After one day, MAPC expansion
media was removed and a serum free media with the sole cytokines 10 ng/mL
FGF-4 and 10 ng/mL HGF was added. Cultures were evaluated 2, 4, 7, 10,
14, 17, 20, and 24 days after culture conditions were switched.
Morphology of the cells changed during the experiment from initially a
spindle, thin shaped cell to a cuboidal, large cell. PAS staining at day
14 demonstrated positive granules similar to that of hepatocytes.
Immunohistochemistry demonstrated that cells stained positive for
cytokeratin (CK)-8 and CK18, HNF-3beta, HNF-4, HNF-1, GATA-4, and albumin
with increasing numbers of cell staining at later time points. By day 24,
approximately 40% of cells stained positive for albumin and CK18. Not all
of these markers are specific for hepatocytes, however taken together they
strongly suggest commitment of these cells towards the hepatocyte lineage.
Quantitative PCR demonstrated a peak of CK19 mRNA expression two days
after addition of the differentiation media which decreased to levels seen
in MAPC. Likewise, levels of HNF-3beta mRNA increased by day 2,
and decreased to level of 5 times higher than in MAPC. We also
showed that MAPC induced to differentiate with FGF-4 and HGF
produced urea from day 4 which increased to day 14 and leveling off
thereafter. The per cell production of urea over time is comparable to
urea production by hepatocytes grown in monolayer. We therefore show that
MAPC's can differentiate in vitro into urea producing
hepatocyte-like cells.

L8 ANSWER 23 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 3
AN 2001:493528 BIOSIS
DN PREV200100493528
TI Isolation of multipotent adult stem cells from the dermis of mammalian
skin.
AU Toma, Jean G. [Reprint author]; Akhavan, Mahnaz [Reprint author];
Fernandes, Karl J. L. [Reprint author]; Barnabe-Heider, Fanie [Reprint
author]; Sadikot, Abbas; Kaplan, David R. [Reprint author]; Miller, Freda

D. [Reprint author]
CS Center for Neuronal Survival, Montreal Neurological Institute, McGill
University, 3801 Rue University, Montreal, PQ, H3A 2B4, Canada
mdfm@musica.mcgill.ca
SO Nature Cell Biology, (September, 2001) Vol. 3, No. 9, pp. 778-784. print.
ISSN: 1465-7392.
DT Article
LA English
ED Entered STN: 24 Oct 2001
Last Updated on STN: 23 Feb 2002
AB We describe here the isolation of stem cells from juvenile and adult
rodent skin. These cells derive from the dermis, and clones of individual
cells can proliferate and differentiate in culture to produce neurons,
glia, smooth muscle cells and adipocytes. Similar precursors that produce
neuron-specific proteins upon differentiation can be isolated from adult
human scalp. Because these cells (termed SKPs for skin-derived
precursors) generate both neural and mesodermal progeny, we propose that
they represent a novel multipotent adult stem
cell and suggest that skin may provide an accessible, autologous
source of stem cells for transplantation.

L8 ANSWER 24 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2002:250146 BIOSIS
DN PREV200200250146
TI Splinkerette-ligated captured T7 (SCT)/RT-PCR, a new method to determine
retroviral integration flanking sequences.
AU Lund, Troy C. [Reprint author]; Lenvik, Todd [Reprint author]; Reyes,
Moryama [Reprint author]; Jiang, Yuehua [Reprint author]; Verfaillie,
Catherine M. [Reprint author]
CS Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 745a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002
AB The ability to determine retroviral integration specific sequences is important in determining clonal expansion in bone marrow transplant, cloning, and the generation of virally transduced clonal cell line. In addition, retroviral marking is often used to demonstrate single stem cell derivation of differentiated cells, in vitro and in vivo. There are several methods described, such as inverse-PCR, two-step PCR, and ligation-mediated PCR. We have developed a PCR assay which is both highly specific and highly sensitive to detect integration specific sequences. This method, termed splinkerette-ligated captured T7 RT-PCR, or SCT/RT-PCR, incorporates several key elements to make it both sensitive and specific: a splinkette linker, magnetic capture of target sequences, and exponential replication of potentially rare sequences using a nested T7 promoter. The target PCR products can be directly sequenced to determine integration sequences. We have successfully determined the integration sequences from as little as 30 pg of provirus containing DNA in the background of 30 ng of untransduced DNA representing a 0.1% transduction rate. We have shown, using retrovirally-marked human multipotent adult stem cells (MASCs), the ability to detect and sequence integration sites (see abstracts from Reyes et al, and Jiang et al). Cells were differentiated along the three primitive embryonic layers, endoderm, mesoderm, and ectoderm. Identical retroviral insertion sites were identified using this technique in the differentiated cells to prove clonal origin. This technique offers investigators great leniency in the amount of DNA and target-rarity in the population of cells being studied. While other techniques have shown 1/1000 clonal cells to be identified, to

our knowledge this is the first technique to identify sequences from as little as 30 pg (10 cells) of DNA in a background of 10,000 cells. This method will aid significantly in determining clonality in transplant experiments as well as the generation of clonal cell populations.

L8 ANSWER 25 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2002:220601 BIOSIS
DN PREV200200220601
TI In vitro and in vivo differentiation of single marrow derived multipotent adult progenitor cell into astrocytes, oligodendrocytes, and functional dopaminergic, serotoninergic or GABA-ergic neurons.
AU Reyes, Morayma [Reprint author]; Verfaillie, Catherine M.; Ortiz, Xilma; Henderson, Dori; Lenvik, Todd
CS Stem Cell Institute, Minneapolis, MN, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 714a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 3 Apr 2002
Last Updated on STN: 3 Apr 2002
AB We have recently described a rare marrow derived cell, termed multipotent adult progenitor cell (MAPC) that can be expanded without obvious senescence ex vivo and can at the single cell level differentiate to osteoblasts, chondroblasts, skeletal myoblasts and endothelial cells. We here demonstrate for the first time that single MAPC from human (h) bone marrow can, depending on the cytokines used, differentiate into oligodendrocytes, astrocytes, and functional, dopaminergic, serotoninergic, or gamma-amino-butyric-acid (GABA)-ergic neurons. Basic-fibroblast growth factor (bFGF) induced hMAPC to differentiate to oligodendrocytes, astrocytes and immature neurons whereas epidermal growth factor and fibroblast growth factor-8b induced differentiation of hMAPC to

GABA-ergic, dopaminergic and serotoninergic neurons but not glia. By cDNA
array, both bFGF-induced and FGF-8b+EGF-induced MAPC expressed many mature neuronal markers such as synaptic proteins and voltage-gated
ion channels. Following coculture with the glioblastoma cell line U-87,
FGF-8b induced neurons matured further and generated tetrodotoxin-sensitive Na-gated voltage action potentials. We used
retroviral marking and PCR analysis for retroviral integration specific
sequences to demonstrate that a single MAPC can differentiate not only into endothelial cells, skeletal myoblast, endodermal cells but
also astrocytes, oligodendrocytes and neurons, indicating the non-neuronal
nature of MAPC. Finally, 1.4X104 undifferentiated hMAPC were transplanted in the ventricles of P1-P3 newborn rats, and rats were
analyzed 4 or 10 weeks later for presence and differentiation of hMAPC in
the brain. At 4 weeks, hMAPC (cell staining positive with an antibody
against human nuclei antibody or human nuclear membrane) had migrated into
the subventicular zone and differentiated into astrocytes (positive
staining for GFAP) and neurons (positive staining for NeuN, MAP-2, and
NF-200). After 12 weeks, hMAPC were found in deeper areas of the brain
such as hippocampus and striatum. Human cells stained positive for NueN
and NF-200. In conclusion, adult marrow derived multipotent progenitor
cells that differentiate into mature functional neurons as well as glial
cells in vitro and in vivo may constitute an extremely valuable source of
cells to treat central nervous system disorders.

L8 ANSWER 26 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2002:220599 BIOSIS
DN PREV200200220599
TI Ex vivo and in vivo primitive hematopoiesis from a non-hematopoietic stem
cell.
AU Reyes, Morayma [Reprint author]; Koodie, Lisa; Jahagirdar, Balkrishna;

Verfaillie, Catherine M.
CS Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 713a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 3 Apr 2002
Last Updated on STN: 3 Apr 2002
AB Multipotent Adult Stem Cells (MASC) from, human bone marrow (BM)
differentiate at the single cell level into neuroectodermal, endodermal
and many mesodermal lineages, including endothelial cells. Because
endothelium and blood are very closely related in ontogeny, we
hypothesized that MASC can differentiate into hematopoietic cells. eGFP
transduced human MASC, that are glycophorin-A (GlyA), CD45 and CD34
negative (n=20), were cocultured with the mouse yolk sac mesodermal cell
line, YSM5, as suspension cell aggregates for 6 days in serum free medium
supplemented with 10 ng/mL bFGF and VEGF. After six days, only eGFP+
cells (MASC progeny) remained and YSM5 cells had died. Remaining cells
were transferred to methylcellulose cultures containing 10% fetal calf
serum supplemented with 10 ng/mL BMP4, VEGF, bFGF, SCF, Flt3L, hyper IL6,
TPO, and EPO for 2 weeks. In these cultures, we detected both adherent
eGFP+ cells and small, round non-adherent cells, which formed many
colonies attached to the adherent cells. The non-adherent and adherent
fractions were collected separately and cultured in 10%FCS containing
medium with 10 ng/mL VEGF and bFGF for 7 days. Adherent cells stained
positive for vWF, formed vascular tubes when plated on ECM, and were able
to uptake a-LDL, indicating their endothelial nature. 5-50% of the

non-adherent cells stained positive for human specific GlyA and HLA-class
I by flow cytometry. Gly-A+/HLA-class-I+ cells were selected by FACS. On
Wright-Giemsa, these cells exhibited the characteristic morphology and
staining pattern of primitive erythroblasts. Cells were benzidine+ and
human Hb+ by immunoperoxidase. By RT-PCR these cells expressed human
specific Hb-e, but not Hb-a. When replated in methylcellulose assay with
20%FCS and EPO, small erythroid colonies were seen after 10 days, and 100%
of these colonies stained positive for human specific GlyA and Hb. As
selection of MASC depends on the depletion of CD45 and Gly A+ cells from
BM, and cultured MASC are CD45- and GlyA- at all times examined using both
FACS and cDNA array analysis, contamination of MASC with hematopoietic
cells is very unlikely. We have showed using PCR that the identical
retroviral integration specific sequences was present in MASC
differentiated to GlyA+ erythroblasts, endodermal, neuroectodermal
endothelial and skeletal muscle cells, proving that a single MASC, which
is of non-hematopoietic origin, differentiates into primitive
erythroblasts, other mesodermal as well as neuroectodermal and endodermal
cell types. When undifferentiated human MASC were transplanted into
NOD/SCID mice, 0.5-5% of human GlyA+/HLA-class I+ were detected in BM and
blood. In conclusion, we demonstrate here for the first time the ex vivo
and in vivo differentiation of non-hematopoietic multipotent stem cells
from adult human BM into primitive erythrocytes as well as other
mesodermal, neuroectodermal and endodermal cell types.

L8 ANSWER 27 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2002:220587 BIOSIS
DN PREV200200220587
TI Characterization of multipotent adult progenitor cells in murine marrow.
AU Jiang, Yuehua [Reprint author]; Reyes, Moryama [Reprint author]; Schwartz,

Robert [Reprint author]; Lenvik, Todd [Reprint author]; Lund, Troy
[Reprint author]; Lisberg, Aaron [Reprint author]; Verfaillie, Catherine
M. [Reprint author]
CS Medicine, Stem Cell Institute, University of Minnesota, Minneapolis, MN,
USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 710a.
print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 3 Apr 2002
Last Updated on STN: 3 Apr 2002
AB Until recent, it was thought that tissue specific stem cells could only
differentiate into cells of the tissue of origin. However, a number of
recent publications have suggested that adult organ specific stem cells
may be capable of differentiating into cells of different tissues. We
have recently shown that a rare cell within mesenchymal stem cell (MSC)
cultures from human marrow can be culture expanded for >80 population
doublings. This cell, termed multipotent adult progenitor cell or
MAPC, differentiates not only into mesenchymal cells but also
endothelium and neuroectoderm. We here describe MAPC from mouse
marrow. We initially used methods identical to those used for human cells
(culture with EGF and PDGF-BB) to isolate and culture expand MASC from
murine marrow, but MAPC could not be isolated. However, when
mouse CD45-/GlyA- cells were cultured in the presence of not only EGF and
PDGF-BB, but also LIF, known to be required for murine but not human ES
cell culture, cultures of CD13+, CD34-, CD44-, class-I and class-II MHC-,
Flk1low MAPC could be established. MAPC have been
maintained for >120 population doublings, without telomere shortening.
Real-time PCR showed presence of Oct4 and Rex1 mRNA, two transcription

factors important in maintaining an undifferentiated status of ES cells.
VEGF induced differentiation of mouse MAPC into endothelium (vWF, Tie, Tek, CD31, CD62E positive) that form vascular tubes in vitro.
In addition differentiation to NF200, MAP2, Tau and NSE positive neurons,
GFAP positive astrocytes and MBP positive oligodendrocytes could be
induced using bFGF. Finally, FGF4 and HGF induced differentiation to
albumin, cytokeratin-18, HNF1 and HNF4 positive hepatocytes, that produce
urea in vitro (abstract Schwartz et al). We have established 'clonal'
cell lines, as shown by retroviral marking studies, and found that
differentiation to mesoderm, ectoderm and endoderm occurs from a single
MAPC. Thus, we identified a subpopulation of MSC that can be
expanded without senescence and differentiates, at the single cell level,
in vitro to mesoderm, neuroectoderm and endoderm. As discussed in other
abstracts, MAPC engraft and differentiate to hematopoietic cells
and epithelial cells in non-injured mice, and contribute to all tissues
when injected in a blastocyst. MAPC therefore hold great
promise for the treatment of congenital or degenerative diseases.

L8 ANSWER 28 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2002:198992 BIOSIS
DN PREV200200198992
TI Engraftment and tissue specific differentiation of multipotent adult
progenitor cells from human marrow in epithelium, the hematopoietic system
and endothelium in vivo.
AU Reyes, Morayma [Reprint author]; Jahagirdar, Balkrishna; Koodie, Lisa;
Verfaillie, Catherine M.
CS Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 547a.
print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of
Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 20 Mar 2002
Last Updated on STN: 20 Mar 2002
AB We have identified a rare marrow derived stem cell, termed multipotent
adult progenitor cell or MAPC, that co-purifies with mesenchymal
stem cells (MSC). Compared with MSC, MAPC can be expanded
significantly more (>100 population doublings) without obvious senescence
ex vivo. In vitro, MAPC can at the single cell level
differentiate to skeletal myoblasts, endothelial cells, neuroectodermal
cells and endodermal cells. In contrast, MSC differentiate only in
mesenchymal cell types. A number of studies have reported that MSC
engraft in mesenchymal tissues, and may engraft in the brain when injected
in the brain parenchyma. As human MAPC have greater
differentiation potential in vitro, we here tested whether they would
engraft in a broader range of tissues in vivo. 106 human MAPC
were injected as a bolus intravenously into non-irradiated NOD/SCID mice.
12 weeks after transplant, mice were sacrificed and multiple organs
analyzed by immunofluoerscence analysis for human specific antigens
(anti-human b2-microglobulin or anti-human nuclei antibodies), and using
tissue specific antibodies to demonstrate in vivo differentiation in
response to organ specific cues. We found 18-25% engraftment of hMAPC in
the crypts and villi of the small intestine. Human cells costained with
an pan-cytokeratin (CK) antibody. In the lung, hMAPC were seen in 27% of
alveoli and 10% of bronchi. Again, human cells co-stained with a pan-CK
antibody. In the liver, human cells could be seen scattered through the
liver parenchyma and some human binucleated cells were seen that
coexpressed pan-cytokeratin at the cellular boundaries. Also in the
liver, MAPC were seen clustered in biliary ducts that double
labeled with a pancytokeratin antibody. Finally, 5%
b2-microglobulin/HLA-class-I positive cells were seen in the bone marrow.

50% of the HLA-class-I+ cells also stained positive with a human specific
anti-Glycophorin-A (GlyA) antibody (indicating erythroid differentiation),
and 30% of the HLA-class-I positive/GlyA negative cells stained positive
for vWF (indicating endothelial differentiation). Up to 10% of cells in
the peripheral blood stained positive for human HLA-class-I and human
GlyA. Finally, human endothelial cells were seen in the vasculature of a
murine, host, thymic lymphoma. Studies are ongoing to determine if
engraftment took place in muscle, heart and brain. In addition, marrow
from primary engrafted animals is being serially transferred to secondary
recipients to determine self renewal occurs of the human cells in vivo.
In conclusion, we report here the engraftment and in vivo differentiation
of human MAPC into epithelial cells of the lung, liver and small
intestine as well as blood and endothelium.

L8 ANSWER 29 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2002:198989 BIOSIS
DN PREV200200198989
TI Multipotent cells derived from adult mouse marrow engraft in a non-injured
recipient and differentiate into hematopoietic, epithelial and endothelial
tissues.
AU Jahagirdar, Balkrishna N. [Reprint author]; Jiang, Yuehua [Reprint
author]; Reyes, Morayma [Reprint author]; Balckstad, Mark [Reprint
author]; Du, Jingbo [Reprint author]; Aldrich, Sara [Reprint author];
Verfaillie, Catherine M. [Reprint author]
CS Stem Cell Institute, University of Minnesota, Minneapolis, MN, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 547a.
print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology,
Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of
Hematology.
CODEN: BLOOAW. ISSN: 0006-4971.

DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 20 Mar 2002
Last Updated on STN: 20 Mar 2002
AB We have identified multipotent cells in post-natal human and murine bone
marrow, termed multipotent adult progenitor cells (MAPC), that differentiate into cells of ectodermal, mesodermal and endodermal origin
in vitro in response to tissue specific cytokines (abstracts Jiang et al).
Here we describe the in vivo behavior of undifferentiated mouse MAPC. 106 MAPC, from beta-galactosidase (b-gal) transgenic ROSA26 mice, were infused via tail vein injection into 4-6
week-old NOD-SCID mice (N=14) with or without sub-lethal irradiation (250
cGy). Animals were sacrificed at 4 to 24 weeks after MAPC injection. Blood, marrow, spleen, liver, intestine, kidney, lung, cardiac
and skeletal muscle and brain of the recipients were analyzed for engraftment of b-gal/Neomycin resistance (NEO) transgene containing cells
by quantitative PCR for NEO and by immunohistochemistry using a FITC
conjugated anti-b-gal antibody. Tissues were co-stained for tissue
specific antigens to confirm in vivo differentiation of the donor MAPC. 1-12% engraftment was seen in marrow, spleen, blood and epithelial tissues of all recipients. No engraftment was seen in skeletal
muscle, myocardium or brain. In all recipients b-gal+ donor cells
expressed markers typical for the tissue in which they had incorporated.
b-gal+ cells in the blood, marrow and spleen co-stained for CD45, TER119,
CD19, Gr1 and Mac1 antigens. In the spleen donor cells were found in
clusters and not as single cells. In the liver, donor cells formed cords
of pan-cytokeratin (CK)+ and albumin+ hepatocytes. In the intestine,
b-gal+/pan-CK+ donor cells covered the epithelial surfaces of the two
villi arising from a single crypt. In the lung alveoli and bronchi with
several b-gal+/pan-CK+ donor cells were found. Irradiation enhanced
MAPC engraftment and differentiation into the hematopoietic

lineage and epithelium of intestine and lung, but had no effect on the degree of engraftment in the liver. Engraftment levels were relatively constant when recipients were analyzed after 4 to 24 weeks. 107 unfractionated marrow cells from two animals with 6-8% engraftment were serially transplanted into 2 secondary recipients following 250 cGy radiation. Chimerism in the secondary recipients was similar to that in the primary hosts. No tumors were seen, except in one animal that developed lymphoma of recipient B-lymphocyte origin. Endothelial cells in the tumor were in part of donor origin. In conclusion, MAPC engraft in non-irradiated and irradiated mice and differentiate in vivo into hematopoietic cells, epithelium of liver, lung and intestine and endothelium. Organs with low cell turnover in the absence of damage, such as skeletal and cardiac muscles, brain, and kidney, did not have donor MAPC engraftment. MAPC may therefore be good source of cells for tissue repair.

L8 ANSWER 30 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN
AN 2002:241253 BIOSIS
DN PREV200200241253
TI The in utero transfer of murine multipotent adult progenitor cells (MAPCs) result in brain and liver differentiation.
AU Tolar, Jakub [Reprint author]; Jiang, Yuehua [Reprint author]; McElmurry, Ron [Reprint author]; Jahagirdar, Balkrishna [Reprint author]; Blackstad, Mark [Reprint author]; Verfaillie, Catherine M. [Reprint author]; Blazar, Bruce R. [Reprint author]
CS Departments of Pediatrics and Medicine, University of Minnesota and Stem Cell Institute, Minneapolis, MN, USA
SO Blood, (November 16, 2001) Vol. 98, No. 11 Part 1, pp. 475a. print.
Meeting Info.: 43rd Annual Meeting of the American Society of Hematology, Part 1. Orlando, Florida, USA. December 07-11, 2001. American Society of Hematology.

CODEN: BLOOAW. ISSN: 0006-4971.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Apr 2002
Last Updated on STN: 17 Apr 2002
AB Recently, we have identified murine MAPCs capable of differentiating in vitro into multiple cell types including cartilage, bone, fat, muscle and endothelium (mesoderm), neuroectoderm and endoderm. We hypothesize that the fetus would represent an ideal setting for in vivo differentiation of MAPCs, consistent with a high proliferative rate of cells within the fetus and widespread cellular migratory patterns which may permit access of MAPCs to sites such as the brain that are not readily accessible post-natally. BALB/c-SCID fetuses were injected at E15/16 with murine MAPCs (3X105 cells) from C57BL/6J-rosa26 (Rosa 26) mice transgenic for lacZ and neomycin resistance (NeoR) genes. Mice were sacrificed 1d (N=3), 8 wks (N=2) and 14 wks (N=3) postnatally. Cryosections were incubated with FITC-conjugated anti beta-galactosidase antibody (LacZ-FITC). Quantitative PCR (qPCR) for NeoR gene expression was performed on sagittal sections of whole mouse mountings obtained from 1d or 8 wk old recipients. qPCR analysis revealed that 1.7% and 12.4% of the total DNA from 8 wk old vs <0.1% of 1d old mice was of Rosa 26 origin, based upon normalization to control murine MAPCs cells. For 14 wk old mice, tissue sections were stained for immunofluorescence and adjacent sections were analyzed by qPCR. Brain engraftment ranged from 0.2 to 1.3% normalized to Rosa 26 MAPC cells, in contrast to the absence of brain engraftment after post-natal MAPC infusion. Using dual color immunofluorescence staining we were able to show co-localization of beta-galactosidase and glial fibrillary acidic protein. Albumin co-staining liver cells derived from Rosa 26 MAPCs were present, albeit infrequently. Analyses are ongoing and will be presented quantifying the potential differentiating

capacity of MAPCs into multiple tissues of mesodermal, ectodermal, and
endodermal origin. In summary, we show for the first time that murine
MAPCs engraft and differentiate into brain and liver cells after in utero
transfer. Our results support the possibility of future clinical use of
MAPCs in attempts to correct neurological, hepatic, and possibly other
types of congenital disorders pre-natally.

L8 ANSWER 31 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2001:486589 BIOSIS
DN PREV200100486589
TI Identification and transplantation of a novel, multipotent neural stem
cell from mammalian skin.
AU Toma, J. G. [Reprint author]; Akhavan, M. [Reprint author]; Fernandes, K.
[Reprint author]; Fortier, M. [Reprint author]; Wang-Ninio, Y. [Reprint
author]; Barnabe-Heider, F. [Reprint author]; Sadikot, A.; Kaplan, D. R.;
Miller, F. D. [Reprint author]
CS Centre for Neuronal Survival, Montreal Neurological Institute, McGill
University, Montreal, PQ, Canada
SO Society for Neuroscience Abstracts, (2001) Vol. 27, No. 1, pp. 57. print.
Meeting Info.: 31st Annual Meeting of the Society for Neuroscience. San
Diego, California, USA. November 10-15, 2001.
ISSN: 0190-5295.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Oct 2001
Last Updated on STN: 23 Feb 2002
AB Here we describe the isolation of neural stem cells from juvenile and
adult rodent skin. These cells, which are called SKPs (SKin-derived
Precursors) derive from the dermis, express nestin and fibronectin, and
can be passaged for over one year without altering their phenotype. When
differentiated in culture, SKPs can generate cells of both neural and
mesodermal origin; neurons, glial cells, smooth muscle cells and

adipocytes. Moreover, clones of single cells can be expanded, and will
still generate all of these different progeny. When transplanted into the
neonatal or adult brain, SKPs survive, migrate, and differentiate into
morphologically complex cells. Finally, similar precursors that express
neuron-specific proteins upon differentiation can be isolated from adult
human scalp. Since these cells are distinct from both CNS-derived neural
stem cells and from mesenchymal stem cells, but can generate both neural
and mesodermal progeny, we propose that they represent a novel
multipotent adult stem cell and
suggest that skin may provide an accessible, autologous source of stem
cells for transplantation.

L8 ANSWER 32 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 2000:505369 BIOSIS
DN PREV200000505369
TI Reliability of an air-braked ergometer to record peak power during a
maximal cycling test.
AU Balmer, James [Reprint author]; Davison, R. C. Richard; Bird, Steve R.
CS Department of Sport Science, Canterbury Christ Church University College,
Canterbury, CT1 1QU, UK
SO Medicine and Science in Sports and Exercise, (October, 2000)
Vol. 32, No. 10, pp. 1790-1793. print.
CODEN: MSPEDA. ISSN: 0195-9131.
DT Article
LA English
ED Entered STN: 22 Nov 2000
Last Updated on STN: 11 Jan 2002
AB Purpose: To assess the reliability of the KingcycleTM ergometer, this
study compared peak power recorded using a Kingcycle and SRMTM power
meters during Kingcycle maximal aerobic power tests. Methods: The study
was completed in two parts: for part 1, nine subjects completed three
maximal tests with a stabilizing kit attached to the Kingcycle rig and
calibration of the Kingcycle checked against SRM (MAPC); and for
part 2, nine subjects completed two maximal tests without the stabilizing

kit and the Kingcycle calibrated using the standard procedure (MAPS).
Each MAPC test was separated by 1 wk; however, MAPS tests were separated by 54 +- 32 d, (mean +- SD). Testing procedure was repeated for
each MAP and peak power output was calculated as the highest average power
output recorded during any 60-s period of the MAP test using the Kingcycle
(KingPPO) and SRM (SRMPPO). Results: Coefficient of variations (CVs) for
KingPPO were larger than those of SRMPPO; 2.0% (95%CI = 1.5-3.0) versus
1.3% (95%CI = 1.0-2.0) and 4.6% (95%CI = 2.7-7.6) versus 3.6% (95%CI =
2.1-6.0) for MAPC and MAPS, respectively. During all tests,
KingPPO was higher than SRMPPO by an average of apprx10% (P < 0.001).
Conclusions: Investigators should be aware of the discrepancy between the
two systems when assessing peak power and that SRM cranks provide a more
reproducible measure of peak power than the Kingcycle ergometer.

L8 ANSWER 33 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 4
AN 2000:32719 BIOSIS
DN PREV200000032719
TI Tumor burden and clonality in multiple intestinal neoplasia mouse/normal
mouse aggregation chimeras.
AU Novelli, Marco R. [Reprint author]; Wasan, Harpreet; Rosewell, Ian; Bee,
Julie; Tomlinson, Ian P.; Wright, Nicholas A.; Bodmer, Walter F.
CS Department of Histopathology, University College London, London, WC1E 6JJ,
UK
SO Proceedings of the National Academy of Sciences of the United States of
America, (Oct. 26, 1999) Vol. 96, No. 22, pp. 12553-12558.
print.
CODEN: PNASA6. ISSN: 0027-8424.
DT Article
LA English
ED Entered STN: 13 Jan 2000
Last Updated on STN: 31 Dec 2001
AB Aggregation chimeras were formed between C57BL/6 mice heterozygous for the
Apcmin (Min) mutation and wild-type SWR mice, that differ in their Pla2g2a
status, a modifier of Apcmin, and also in their resistance to intestinal

polyp formation. Variation in the dolichos biflorus agglutinin-staining
patterns of the intestines of these mouse strains was used to determine
the chimeric composition of the intestine in individual mice and to
examine the clonal composition of adenomas. Macroscopic adenoma numbers
in chimeric mice were compared with the expected adenoma numbers based on
the percentage of C57BL/6J-Apcmin/+ epithelium in individual mice. These
results unexpectedly show that there was no apparent inhibitory effect of
the SWR-derived (Pla2g2a wild-type) tissue on adenoma formation in the
C57BL/6J-Apcmin/+ epithelium. This suggests that the main genetic
modifiers of the Min phenotype act at a cellular or crypt-restricted level
with no discernable systemic effect. All adenomas were seen to contain
C57BL/6J-Apcmin/+-derived epithelium, confirming that the germ-line
mutation of the mApc gene is necessary to initiate tumorigenesis
in this model system, and that the mApc gene acts in a cell
autonomous fashion.

L8 ANSWER 34 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 5
AN 2000:14771 BIOSIS
DN PREV200000014771
TI The effect of the chemical structure of the phospholipid polymer on
fibronectin adsorption and fibroblast adhesion on the gradient
phospholipid surface.
AU Iwasaki, Yasuhiko [Reprint author]; Sawada, Shin-ichi; Nakabayashi, Nobuo;
Khang, Gilson; Lee, Hai Bang; Ishihara, Kazuhiko
CS Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental
University, 2-3-10 Kanda-surugadai, Chiyoda-ku, Tokyo, 101-0062, Japan
SO Biomaterials, (Nov., 1999) Vol. 20, No. 22, pp. 2185-2191.
print.
CODEN: BIMADU. ISSN: 0142-9612.
DT Article
LA English
ED Entered STN: 29 Dec 1999
Last Updated on STN: 31 Dec 2001
AB The interaction between biocomponents and the polyethylene (PE) surface

modified with poly(omega-methacryloyloxyalkyl phosphorylcholine (MAPC)) was considered taking into account the surface characteristics, i.e., density, mobility, and orientation of the poly(MAPC). The PE surface, grafted gradually with the poly(MAPC) was prepared by corona irradiation method. The amount of peroxide produced on the PE surface which was determined with 1,1-diphenyl-2-picryl-hydrazyl, increased with an increase in the energy of the corona. The surface density of the poly(MAPC) was increased with an increase in the amount of the peroxides produced by the corona irradiation. The orientation and mobility of the poly(MAPC) grafted on the PE surface was evaluated with 1,6-diphenyl-1,3,5-hexatriene. The orientation of the poly(6-methacryloyloxyhexyl phosphorylcholine (MHPC)) which has six methylene chains between the phospholipid polar group and the backbone was higher than that of other poly(MAPC)s. The mo bility of the poly(MAPC) decreased with an increase in the methylene chain length in the MAPC unit. The fibronectin adsorption on the gradient PE sheet grafted with poly(MAPC) was determined with enzyme-labeled immunoassay. The amount of adsorbed fibronectin on the PE grafted with poly(2-methacryloyloxyethyl phospohorylcholine(MPC)) and poly(MHPC) decreased with an increase in their surface density. Especially, the PE sheet grafted with the poly(MHPC) was effectively reduced compared with other poly(MAPC)s. On the poly(10-methacryloyloxydecyl phosphorylcholine (MDPC)), there is a minimum amount of adsorbed fibronectin. The fibronectin adsorption pattern on the PE sheet grafted with poly(MAPC) was quite different from the chemical structure of the MAPC unit. The human normal diploid fibroblasts (WI-38 cells) were cultured on the gradient PE sheet grafted with poly(MAPC) changing the concentration of seeded WI-38 cells. The adhesion behavior of the WI-38 cells was different depending on the concentration of the seeded WI-38 cells. When the concentration was low, the number of the adherent WI-38 cells had the same tendency as fibronectin adsorption. The gradient PE sheet grafted with the poly(MHPC) effectively reduced WI-38 cells adhesion even when the concentration of the WI-38 cells was high. The biocompatibility of polymer surfaces can be

improved by highly oriented phosphorylcholine group.

L8 ANSWER 35 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1999:392330 CAPLUS
DN 131:35798
TI Surface modified poly(methyl methacrylate) with 1-methyl-2-methacrylamidoethyl phosphorylcholine moiety
AU Sugiyama, Kazuo; Ohga, Koji
CS Dep. Industrial Chemistry, Faculty Engineering, Kinki Univ., Higashi-Hiroshima, 739, Japan
SO Macromolecular Chemistry and Physics (1999), 200(6), 1439-1445
CODEN: MCHPES; ISSN: 1022-1352
PB Wiley-VCH Verlag GmbH
DT Journal
LA English
AB A series of poly(Me methacrylate) [poly(MMA)] microspheres covered with the 1-methyl-2-methacrylamidoethyl phosphorylcholine (MAPC) moiety, poly(MAPC-co-MMA), were prepared by emulsifier-free emulsion copolymn. of Me methacrylate (MMA) and MAPC using potassium peroxo-disulfate (KPS) or 2,2'-azobis[2-(imidazolin-2-yl)propane] dihydrochloride (ABIP) as initiators. The ζ-potentials of the particles are -72 to -26 mV and 0 to 27 mV for poly(MAPC-co-MMA) produced by KPS and ABIP, resp. Poly(MAPC-co-MMA) suppresses the adsorption of albumin, γ-globulin, and fibrinogen more than poly(MMA) as the control. From XPS measurements the MAPC moiety and the fragments of the initiator are located on the surface of the polymer films prepared from poly(MAPC-co-MMA). Egg yolk lecithin adsorbs on the surface of the films, and an organized adsorption layer of lipid, i.e., a hydrogel layer with an analogous structure to biomembrane, is formed.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 36 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 6
AN 1999:300283 BIOSIS
DN PREV199900300283
TI Competitive adsorption between phospholipid and plasma protein on a phospholipid polymer surface.
AU Iwasaki, Yasuhiko [Reprint author]; Nakabayashi, Nobuo; Nakatani, Masako; Mihara, Takashi; Kurita, Kimio; Ishihara, Kazuhiko
CS Institute for Medical and Dental Engineering, Tokyo Medical and Dental University, 2-3-10, Kanda-surugadai, Chiyoda-ku, Tokyo, 101-0062, Japan

SO Journal of Biomaterials Science Polymer Edition, (1999) Vol. 10, No. 5, pp. 513-529. print.
CODEN: JBSEEA. ISSN: 0920-5063.
DT Article
LA English
ED Entered STN: 12 Aug 1999
Last Updated on STN: 12 Aug 1999
AB The competitive adsorption of proteins and phospholipids on omega-methacryloyloxyalkyl phosphorylcholine (MAPC) polymer was evaluated in this study. Albumin, fibrinogen, and dimyrstoyl phosphatidylcholine (DMPC) were used as model components. The amount of DMPC adsorbed on the MAPC polymers increased with an increase in the MAPC unit composition of the polymer. The methylene chain length of the MAPC unit was another factor influencing the DMPC adsorption when the MAPC unit composition of the MAPC polymer was low. The state of albumin and DMPC liposome adsorbed on the 2-methacryloyloxyethyl phosphorylcholine (MPC) polymer was determined by dynamic contact angle (DCA) measurement. The adsorption strength of albumin on the MPC polymer was weaker than that on the poly(n-butyl methacrylate (BMA)), that is, the albumin was detached from the MPC polymer during the rinsing process. On the poly(BMA) surface, no difference in the shape of the DCA loops before and after contact with the DMPC liposomal suspension was observed. Fibrinogen adsorption on the MAPC polymer was detected by gold-colloid labeled immunoassay. The amount of fibrinogen adsorbed on every MAPC polymer surface was reduced by addition of the DMPC liposome in the fibrinogen solution. The number of platelets adhered on the MAPC polymer was also decreased when the DMPC liposome was present in the fibrinogen solution during pretreatment. We concluded that phospholipids were preferentially adsorbed on the MAPC polymer surface compared with plasma protein and that the adsorbed phospholipids played an important role in showing an excellent blood compatibility on the MAPC polymer.

L8 ANSWER 37 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 7
AN 1999:342613 BIOSIS
DN PREV199900342613
TI Behavior of blood cells in contact with water-soluble phospholipid

polymer.
AU Iwasaki, Yasuhiko [Reprint author]; Ijuin, Mika; Mikami, Asako; Nakabayashi, Nobuo; Ishihara, Kazuhiko
CS Institute of Biomaterials and Bioengineering, Tokyo Medical and Dental University, 2-3-10, Kanda-Surugadai, Chiyoda-ku, Tokyo, 101-0062, Japan
SO Journal of Biomedical Materials Research, (Sept. 5, 1999) Vol. 46, No. 3, pp. 360-367. print.
CODEN: JBMRBG. ISSN: 0021-9304.
DT Article
LA English
ED Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999
AB omega-Methacryloyloxyalkyl phosphorylcholine (MAPC) polymer, which has various methylene chain lengths between the phosphorylcholine group and the backbone, was synthesized with attention to formation of the biomembrane. The effect of water-soluble poly(MAPC) on the function and activation of blood cells was evaluated to determine the interaction between blood cells and the MAPC polymer. The poly(MAPC) and the MAPC copolymer with a small amount of fluorescent units were synthesized by a conventional radical polymerization technique. Using a fluorescence spectrometer, it was determined that the MAPC polymer was adsorbed on the plasma membrane of platelets when the platelets were suspended in an aqueous solution of the MAPC copolymer. The hemolytic activity of poly(MAPC) was less than that of other water-soluble polymers, such as poly(ethylene glycol) and poly(1-vinyl-2-pyrrolidone) (PVPy). The change in the plasma membrane fluidity of platelets on contact with poly(MAPC) was determined with 1,6-diphenyl-1,3,5,-hexatriene. The plasma membrane fluidity of platelets decreased with an increase in the methylene chain length of the MAPC unit. The aggregation activity of platelets after contact with poly(MAPC) was also evaluated, but no significant difference between that of polymer-contacted platelets and native platelets was observed. Finally, the activity of platelets on contact with poly(MAPC) was determined by measuring the cytoplasmic calcium ion concentration ((Ca2+)i) in platelets. The increase in (Ca2+)i in the platelets after contact with poly(MAPC) was similar to that of native platelets. We conclude that the poly(MAPC) reduced platelet activation even though the poly(

MAPC) adsorbed on the membrane surface of the platelets. In particular, poly(10-methacryloyloxydecyl phosphorylcholine) significantly reduced platelet activation compared with PVPy.

L8 ANSWER 38 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2000:42367 CAPLUS
DN 132:66084
TI A state space model based multistep adaptive predictive controller (
MAPC) with disturbance modeling and Kalman filter prediction
AU Sripada, N. Rao; Fisher, D. Grant
CS Department of Chemical Engineering, Indian Institute of Technology,
Madras, 600 036, India
SO Indian Journal of Chemical Technology (1999), 6(4), 225-236
CODEN: ICHTEU; ISSN: 0971-457X
PB National Institute of Science Communication, CSIR
DT Journal
LA English
AB A multistep adaptive predictive control strategy based on a state space
model of the process has been developed. It can be compared with the
generalized predictive control algorithm. The emphasis in the development
of the proposed control scheme is on modeling and elimination of
disturbances. In the proposed scheme any prior information regarding the
disturbances can be incorporated (by specifying certain polynomials and/or
the noise covariances). If no prior information is available then the
unknown un-modeled effects (such as noise, unmeasured load-disturbances
and model process mismatch) can be represented by a residual model which
can best be identified in a two-stage setting. This approach leads to
satisfactory modeling of disturbances and good regulation via predictive
control. Some important features of the proposed algorithm are: (i) it
uses a state space model which allows sep. modeling of u-to-y process
dynamics, process and measurement noise; this is not possible in an
ARMAX-type input/output model where process and measurement noise appear
lumped in the noise polynomial; (ii) it uses a Kalman Filter (KF) to
generate the predictions of the output; the KF can be easily tuned via

noise covariances and is a simpler and better alternative to specifying or
estimating a noise polynomial; (iii) there is no need to solve a Diophantine
identity online; the result is reduced computation; and (iv) if residual
modeling is used it leads to simpler and improved way of handling
disturbances. The proposed control algorithm is presented for the
single-input, single-output case. Applying the algorithm to multivariable
processes is straightforward. Simulation examples are included to
illustrate the advantages and performance of the proposed control scheme.
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 39 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN
AN 1999:308399 BIOSIS
DN PREV199900308399
TI Polyp number and clonality in multiple intestinal neoplasia mouse
aggregation chimaeras.
AU Novelli, M. R. [Reprint author]; Wasan, H.; Rosewell, I.; Bee, J.;
Tomlinson, I. A.; Wright, N. A.; Bodmer, W. F.
CS Department of Histopathology, University College London, London, UK
SO Journal of Pathology, (1999) Vol. 187, No. SUPPL., pp. 34A.
print.
Meeting Info.: 178th Meeting of the Pathological Society of Great Britain
and Ireland. Cambridge, England, UK. January 6-8, 1999. Pathological
Society of Great Britain and Ireland.
CODEN: JPTLAS. ISSN: 0022-3417.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 12 Aug 1999
Last Updated on STN: 12 Aug 1999

L8 ANSWER 40 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 8
AN 1998:429072 BIOSIS
DN PREV199800429072
TI Platelet adhesion on the gradient surfaces grafted with phospholipid
polymer.

AU Iwasaki, Yasuhiko [Reprint author]; Ishihara, Kazuhiko; Nakabayashi,
Nobuo; Khang, Gilson; Jeon, Ju Hyeong; Lee, Jin Whan; Lee, Hai Bang
CS Inst. Med. Dent. Eng., Tokyo Med. Dent. Univ., 2-3-10 Kanda-Surugadai,
Chiyoda-ku, Tokyo 101-0062, Japan
SO Journal of Biomaterials Science Polymer Edition, (1998) Vol. 9, No. 8, pp. 801-816. print.
CODEN: JBSEEA. ISSN: 0920-5063.
DT Article
LA English
ED Entered STN: 7 Oct 1998
Last Updated on STN: 7 Oct 1998
AB We have synthesized omega-methacryloyloxyalkyl phosphorylcholine (
MAPC) polymers as new blood-compatible materials, with attention to the surface structure of the biomembrane and investigated their blood
compatibility. The blood compatibility observed on the MAPC polymers is due to their strong affinity to phospholipids. When the blood
comes in contact with the MAPC polymer, phospholipids in the plasma preferentially adsorb on the surface, compared with the plasma
proteins or cells. The adsorbed phospholipids construct a biomembrane-like structure on the MAPC polymer surface. The
MAPC polymers then have an excellent blood compatibility. In this
study, we prepared a gradient poly(MAPC)-grafted polyethylene (PE) surface using a corona discharge treatment method to clarify the
effect of the chemical structure of the MAPC unit on the blood compatibility of the MAPC polymers. The surface composition of
MAPC and the hydrophilicity on the poly(MAPC)-grafted PE surface were determined by X-ray photoelectron spectroscopic (XPS)
analysis and contact angle measurement with water, respectively. The
phosphorus/carbon (P/C) ratio determined by the XPS analysis increased,
but the water contact angle decreased with increasing corona irradiation
energy. These results indicated that the surface density of the MAPC unit was increased. More than 2.5 cm from the starting point
of the corona irradiation, the P/C ratio and water contact angle of the
surface achieved a constant level. Thus, the surface was completely
covered with the grafted poly(MAPC) chain. The effect of the methylene chain length of the MAPC unit on surface properties

was also observed. The phospholipid polar group of the MAPC unit was effectively exposed on the surface as the chain length became longer. Moreover, the hydrophobicity of the surface was increased with the increase in the methylene chain length of the MAPC unit. The number of platelets adhering to the poly(MAPC)-grafted PE surface was reduced from the same point where the P/C ratio became constant.

L8 ANSWER 41 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 9
AN 1998:485747 BIOSIS
DN PREV199800485747
TI Desethylamiodarone prolongation of cardiac repolarization is dependent on gene expression: A novel antiarrhythmic mechanism.
AU Drvota, Viktor [Reprint author]; Blange, Irina; Haggblad, Johan; Sylven, Christer
CS Dep. Cardiol., M52, Huddinge Univ. Hosp., S-141 86 Huddinge, Sweden
SO Journal of Cardiovascular Pharmacology, (Oct., 1998) Vol. 32, No. 4, pp. 654-661. print.
CODEN: JCPCDT. ISSN: 0160-2446.
DT Article
LA English
ED Entered STN: 5 Nov 1998
Last Updated on STN: 5 Nov 1998
AB Desethylamiodarone (DEA) is the major metabolite of amiodarone and has similar electrophysiologic effects with prolongation of the repolarization that is reversed by thyroid hormone (T3). Some of the electrophysiologic effects are probably due to antagonism of T3 at the receptor level. Such effects of T3 are mediated by modulation of gene transcription. The aim of this study was to investigate whether cycloheximide (Cy), an inhibitor of protein synthesis, and actinomycin D (ActD), a RNA-synthesis inhibitor, block DEA-induced prolongation of the repolarization and whether DEA takes part in the autoregulation of the nuclear thyroid hormone-receptor subtypes (ThR). Corrected monophasic action potentials (MAPc) and QTc were measured in Langendorff-perfused guinea pig hearts for 1 h.

The hearts were continuously perfused with (a) vehicle, (b) 7.5 muM Cy, (c) 5 muM DEA, (d) 5 muM DEA + 7.5 WV Cy, (e) 1 muM T3, (f) 5 muM DEA + 1 muM T3, (g) 1.5 muM ActD, and (h) ActD + DEA. A potassium channel blocker with class III antiarrhythmic effects, 0.5 muM almokalant, was used as a control, separately and together with Cy. Western blot analysis for the ThR subtypes a, beta1, and beta2 was performed on vehicle and DEA-treated hearts. DEA increased MAPc by 19% ($p < 0.0005$) and QTc by 18% ($p < 0.0005$). There was no effect on MAPc or QTc when Cy, ActD, or T3 was added with DEA. Almokalant increased MAPc by 14% ($p < 0.005$) and QTc by 13% ($p < 0.0005$). When Cy was present, almokalant still induced a similar prolongation of MAPc by 14% ($p < 0.005$) and QTc by 17% ($p < 0.0005$). Western blot analysis revealed no change in the expression of the ThR protein. In conclusion, the prolongation of the cardiac repolarization by DEA, but not almokalant, can be totally blocked by Cy and ActD. This indicates that the class III action of DEA is at least in part dependent on transcription rather than a direct effect on cell-membrane channels or receptors. The action of DEA could be reversed by T3, indicating an antagonism between DEA and T3.These results suggest a new antiarrhythmic mechanism dependent on gene expression.

L8 ANSWER 42 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on STN DUPLICATE 10

AN 1997:434403 BIOSIS

DN PREV199799733606

TI Reduction of surface-induced platelet activation on phospholipid polymer.

AU Iwasaki, Yasuhiko [Reprint author]; Mikami, Asako; Kurita, Kimio; Yui, Nobuhiko; Ishihara, Kazuhiko; Nakabayashi, Nobuo

CS Inst. Med. Dental Engineering, Tokyo Med. Dental Univ., 2-3-10 Kanda-surugadai, Chiyoda-ku, Tokyo 101, Japan

SO Journal of Biomedical Materials Research, (1997) Vol. 36, No. 4, pp. 508-515.
CODEN: JBMRBG. ISSN: 0021-9304.

DT Article

LA English

ED Entered STN: 8 Oct 1997

Last Updated on STN: 21 Nov 1997

AB omega-Methacryloyloxyalkyl phosphorylcholine (MAPC) polymers which have been synthesized with attention to the surface structure of a biomembrane show excellent blood compatibility, i.e., resistance to protein adsorption and blood cell adhesion. To clarify the stability of platelets in contact with the MAPC polymer surfaces, cytoplasmic free calcium concentration ((Ca-2+)-i) in the platelets was measured. A platelet suspension was passed through a column packed with various polymer beads after treatment with plasma, and the (Ca-2+)-i in the platelets eluted from the column was measured. The (Ca-2+)-i in contact with the MAPC polymers, i.e., poly(2-methacryloyloxyethyl phosphorylcholine-co-n-butyl methacrylate (BMA)) (PMEB) and poly(6-methacryloyloxyhexyl phosphorylcholine-co-BMA) (PMHB), was less than that in contact with poly(BMA). However, poly(10-methacryloyloxydecyl phosphorylcholine-co-BMA) (PMDB) was not effective in suppressing the increase in (Ca-2+)-i, and thus was at the same level as in the poly(BMA). This result indicated that platelets in contact with PMEB or PMHB were less activated compared with those in contact with PMDB and poly(BMA). Moreover, the state of the platelets adhered to these polymer surfaces, both morphologically and immunologically, was examined. Scanning electron microscopic observation of the polymer surface after contact with a platelet suspension revealed that many platelets adhered and changed their shape on the poly(BMA). The numbers of adherent platelets were reduced on all MAPC polymer surface. The relative amount of alpha-granule membrane glycoprotein (GMP-140) which appears on the cell membrane by activation of platelets on the PMEB surfaces was less than that on poly(BMA) and poly(2-hydroxyethyl methacrylate). These results suggest that PMEB and PMHB suppressed not only platelet adhesion but also activation of the platelets in contact with these surfaces.

L8 ANSWER 43 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN DUPLICATE 11
AN 1997:615547 CAPLUS
DN 127:336526
OREF 127:65999a,66002a
TI Stabilization of liposomes attached to polymer surfaces having phosphorylcholine groups
AU Iwasaki, Yasuhiko; Tanaka, Shinobu; Hara, Masahiko; Ishihara, Kazuhiko; Nakabayashi, Nobuo
CS Inst. Med. and Dental Eng., Tokyo Med. and Dental Univ., Tokyo, 101, Japan
SO Journal of Colloid and Interface Science (1997), 192(2), 432-439
CODEN: JCISA5; ISSN: 0021-9797
PB Academic
DT Journal
LA English
AB The adsorption state of liposomes on a polymer surface containing a phosphorylcholine group, i.e., ω-methacryloyloxyalkyl phosphorylcholine (MAPC) polymer, was evaluated using a quartz crystal microbalance and an atomic force microscope. After a quartz crystal resonator coated with the MAPC polymer or poly[2-hydroxyethyl methacrylate (HEMA)] was equilibrated with distilled water, the quartz crystal was contacted with a dipalmitoylphosphatidylcholine (DPPC) liposomal suspension. The resonance frequency change during liposome adsorption on the poly(HEMA)-coated resonator was larger than that on the MAPC polymer-coated resonator. The temperature response based on the phase transition of adsorbed DPPC liposomes, i.e., the liquid crystalline state to gel state, on the MAPC polymer-coated resonator was more sensitive than that on the poly(HEMA)-coated resonator. Moreover,when the DPPC liposomes adsorbed on the polymer surfaces were disintegrated with a nonionic surfactant, it took longer for the frequency to return to the initial value of the poly-(HEMA)-coated resonator than to that of the MAPC polymer-coated resonator. According to atomic force microscopic observation of the polymer surface after treatment with the liposomal suspension, the DPPC liposomes adsorbed on the MAPC polymers maintained their spherical shape well. We conclude that DPPC liposomes adsorbed on the poly(HEMA) surface can penetrate a hydrated layer and its

ordered structure. On the other hand, DPPC liposomes may adsorb to the
MAPC polymer surface without change in their original structure.
RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 44 OF 88 EMBASE COPYRIGHT (c) 2009 Elsevier B.V. All rights
reserved on STN
AN 1997141519 EMBASE
TI Two-component signal transducers and MAPK cascades.
AU Wurgler-Murphy, Susannah M. (correspondence); Saito, Haruo
CS Division of Tumor Immunology, Dana-Farber Cancer Institute, Harvard
Medical School, Boston, MA 02115, United States.
haruo_saito@dfci.harvard.
edu
AU Wurgler-Murphy, Susannah M. (correspondence)
CS Division Tumor Immunology, Dana-Farber Cancer Institute, Boston, MA 02115,
United States.
SO Trends in Biochemical Sciences, (May 1997) Vol. 22, No. 5, pp. 172-176.
Refs: 38
ISSN: 0968-0004 CODEN: TBSCDB
PUI S 0968-0004(97)01036-0
CY United Kingdom
DT Journal; General Review; (Review)
FS 029 Clinical and Experimental Biochemistry
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LA English
SL English
ED Entered STN: 29 May 1997
Last Updated on STN: 29 May 1997
AB Two-component signal transducers, which are characterized by the
histidine-to-aspartate phospho-transfer mechanism, were once thought to be
restricted to prokaryotes. They have, however, now been identified in
diverse eukaryotic species including plant, fungus, yeast and slime mold,
In yeast, a two-component osmosensor has been found to regulate a
mitogen-activated protein kinase (MAPC) cascade, a ubiquitous
eukaryotic signaling module.

L8 ANSWER 45 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 12
AN 1997:38257 BIOSIS
DN PREV199799330245
TI Effect of reduced protein adsorption on platelet adhesion at the

phospholipid polymer surfaces.
AU Iwasaki, Yasuhiko; Kurita, Kimio; Ishihara, Kazuhiko [Reprint author];
Nakabayashi, Nobuo
CS Inst. Med. Dental Engineering, Tokyo Med. Dental Univ., 2-3-10 Kanda-surugadai, Chiyoda-ku, Tokyo, 101, Japan
SO Journal of Biomaterials Science Polymer Edition, (1996) Vol. 8, No. 2, pp. 151-163.
CODEN: JBSEEA. ISSN: 0920-5063.
DT Article
LA English
ED Entered STN: 28 Jan 1997
Last Updated on STN: 25 Mar 1997
AB We prepared polymers having a phospholipid polar group, poly(omega-methacryloyloxyalkyl phosphorylcholine (MAPC)-co-n-butyl methacrylate(BMA)), as new biomedical materials and evaluated their blood compatibility with attention to protein adsorption and platelet adhesion. The total amount of proteins adsorbed on the polymer surface from human plasma was determined, and the distribution of adsorbed proteins on the plasma-contacting surface was analyzed. The amount of proteins adsorbed on every poly(MAPC-co-BMA) was small compared with that observed on polymers without the phospholipid polar group. However, there was no significant difference in the amount of adsorbed proteins on the poly(MAPC-co-BMA) even when the methylene chain length between the phospholipid polar group and the backbone in the MAPC moiety was altered. Platelet adhesion on the polymer surface from a platelet suspension in a buffered solution was evaluated with and without plasma treatment on the surface. When a rabbit platelet suspension was brought into contact with the poly(BMA) surface after treatment with plasma, many platelets adhered and aggregated. However, a reduced amount of platelet adhered on the poly(BMA) was found in the case of direct contact with the platelet suspension. On the other hand, the poly(MAPC-co-BMA)s could inhibit platelet adhesion under both conditions. Based on these results, it can be concluded that the proteins adsorbed on the surface play an important role in determining the platelet adhesion and suppression of the protein adsorption on the surface, which

is one of the most significant ways of inhibiting platelet adhesion.

L8 ANSWER 46 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1997:200473 CAPLUS
DN 126:248973
OREF 126:48087a,48090a
TI O2-dependent electron flow in intact spinach chloroplasts: properties and
possible regulation of the Mehler-ascorbate peroxidase cycle
AU Schreiber, Ulrich; Hormann, Henning; Asada, Kozi; Neubauer, Christian
CS Lehrstuhl Botanik I, Universitat Wurzburg, Wurzburg, D-97082, Germany
SO Photosynthesis: From Light to Biosphere, Proceedings of the International
Photosynthesis Congress, 10th, Montpellier, Fr., Aug. 20-25, 1995 (
1995), Volume 2, 813-818. Editor(s): Mathis, Paul. Publisher: Kluwer, Dordrecht, Neth.
CODEN: 64DFAW
DT Conference
LA English
AB A brief overview on the properties of the Mehler-ascorbate peroxidase
cycle (MAPC) proves it to be particularly effective in the
formation of a regulatory ΔpH in intact spinach chloroplasts. The
effects of low concns. of the uncoupler nigericin on O2-dependent electron
flow and on ΔpH formation indicate that the suppression of electron
flow and of the ΔpH associated with MAPC activity occurs at
.apprx.10-fold lower nigericin concn than the stimulation of Me
viologen-catalyzed O2-reduction The effect of ADP-addition on O2-dependent flow
and on the associated ΔpH in class D chloroplasts in the presence of
other acceptors further supports the possibility of MAPC
regulation by the energy-status of the thylakoids. The requirements of O2
and ascorbate for ΔpH-formation in intact chloroplasts favor a major
role of O2 in ΔpH-formation by the MAPC. In conclusion,
substantial evidence has been accumulated suggested that O2-dependent
electron flow in the MAPC has the potential of generating a
large ΔpH in intact spinach chloroplasts.

L8 ANSWER 47 OF 88 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1995:684452 CAPLUS
DN 123:123027

OREF 123:21697a,21700a
TI Ex vivo blood compatibility of polymers having phospholipid polar group
AU Iwasaki, Yasuhiko; Kurita, Kimio; Tanaka, Shinobu; Ishihara, Kazuhiko;
Nakabayashi, Nobuo
CS College Science and Technology, Nihon University, Tokyo, 101, Japan
SO Seitai Zairyo (1995), 13(2), 62-9
CODEN: SEZAEH; ISSN: 0910-304X
PB Nippon Baiomateriaru Gakkai
DT Journal
LA Japanese
AB We have already reported the effects of hydrophobicity of phospholipid
moiety on hemocompatibility, phospholipid polymers (MAPC copolymer) with various methylene chain length between the phosphorylcholine group and main chain of the copolymer were prepared and
their characteristics were evaluated with attention to the phospholipid
and protein adsorptions, and platelet adhesion. In this study, in order
to evaluate an availability of the MAPC copolymers as coating materials for poly(vinyl chloride)(PVC), which is commonly used in extra
corporeal circuit, such as tubing, reservoirs, connectors etc, hemocompatibility of PVC coated with MAPC copolymer was evaluated through in vitro tests and ex vivo shunt expts. When platelet-rich plasma (PRP) was contacted with PVC for 60 min, a lot of
platelets adhered and activated, On the MAPC copolymer of 0.1 MAPC mole fraction, the number of platelet adhered decreased with an
increase in the methylene chain length. On the other hand, when MAPC mole fraction was increased to 0.3, platelet adhesion was completely suppressed. The similar tendency of the platelet adhesion with
respect to the methylene chain length was observed when PRP was contacted
with the surface of poly (BMA) coated with MAPC copolymer of 0.1 mol fraction for 180 min. Regarding the ex vivo tests, carotid artery-venous shunt expts. were carried out using rabbits and it was
confirmed that after 30 min' circulation, a lot of platelets adhered on
the MAPC coated PVC surface compared with the results obtained in vitro tests. But the number of platelet adhered also decreased with an
increase in the methylene chain length.

L8 ANSWER 48 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on

STN DUPLICATE 13
AN 1994:494318 BIOSIS
DN PREV199497507318
TI Effect of methylene chain length in phospholipid moiety on blood compatibility of phospholipid polymers.
AU Iwasaki, Y.; Kurita, K.; Ishihara, K. [Reprint author]; Nakabayashi, N.
CS Inst. Med. Dent. Eng., Tokyo Med. Dent. Univ., 2-3-10, Kanda-surugadai, Chiyoda-ku, Tokyo 101, Japan
SO Journal of Biomaterials Science Polymer Edition, (1994) Vol. 6, No. 5, pp. 447-461.
CODEN: JBSEEA. ISSN: 0920-5063.
DT Article
LA English
ED Entered STN: 28 Nov 1994
Last Updated on STN: 29 Nov 1994
AB To investigate the effects of the methylene chain length between the phospholipid polar group and the backbone on blood compatibility of a phospholipid polymer, copolymers of omega-methacryloyloxyalkyl phosphorylcholine (MAPC) with n-butyl methacrylate (BMA) were synthesized. The methylene chains were ethylene (n = 2), tetramethylene (n = 4), and hexamethylene (n = 6). Every MAPC copolymer with an MAPC mole fraction in the range of 0.1-0.3 was soluble in ethanol but only swelled in water, and the equilibrium water fraction of the water-swollen MAPC copolymer membrane decreased with the length of the methylene chain. When a rabbit platelet-rich plasma was applied on the MAPC copolymer surface with an 0.1 MAPC mol fraction for 180 min, the number of adhered platelets depended on the length of the methylene chain in the MAPC moiety of the copolymer. The amount of phospholipid adsorbed on the MAPC copolymer from human plasma was larger than that on hydrophobic poly(BMA) and increased with the length of the methylene chain in the MAPC moiety. That is, the reduction of platelet adhesion corresponded to the increase in the amount of phospholipid adsorbed on the MAPC copolymer.

L8 ANSWER 49 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 14
AN 1994:276227 BIOSIS
DN PREV199497289227
TI Effects of 4-MAPC, a 5-alpha-reductase inhibitor, and cyproterone acetate on regrowth of the rat ventral prostate.

AU Shao, Tsang C.; Kong, Ann; Cunningham, Glenn R. [Reprint author]
CS ACOS Res. and Dev., VA Med. Cent., 2002 Holcombe Blvd., Houston, TX 77030,
USA
SO Prostate, (1994) Vol. 24, No. 4, pp. 212-220.
CODEN: PRSTDS. ISSN: 0270-4137.
DT Article
LA English
ED Entered STN: 24 Jun 1994
Last Updated on STN: 25 Jun 1994
AB Inhibitors of 5-alpha-reductase activity cause less involution of the rat
ventral prostate (VP) than does castration. Studies were conducted in
adult Sprague Dawley rats to evaluate the effects of a potent
5-alpha-reductase inhibitor, 4-MAPC, and the antiandrogen,
cyproterone acetate (CA), on DNA synthesis and apoptosis. In experiment
1, VP weight fell 33%, 53%, and 83%, and DNA per ventral prostate was
reduced 24%, 46%, and 71%, by 4-MAPC, CA, and castration,
respectively. In experiment 2, adult rats were castrated, and the VP
involuted for 7 days prior to 3 daily injections of testosterone
propionate (TP; 1 mg/kg/d) +- 10 mg/kg/d of 4-MAPC or CA.
3H-thymidine incorporation into VP DNA was increased in castrated animals
treated with TP, and 4-MAPC and CA reduced uptake. In
experiment 3, animals were treated for 14 days with the same protocol as
that used in experiment 2. VP weight was increased in all animals treated
with TP when compared with castration, and was reduced by both 4-MAPC and CA. DNA in rats treated with TP was similar to that in
intact animals. DNA was not reduced by 4-MAPC, but was reduced
by CA. The mRNA for TRPM-2, a marker of apoptosis, was increased only in
untreated castrated rats. It appears that CA has a greater inhibitory
effect than 4-MAPC on DNA synthesis. A major reason why
castration reduces DNA more than either 4-MAPC or CA is that
neither of these agents was able to increase programmed cell death to the
degree seen with castration.

L8 ANSWER 50 OF 88 BIOSIS COPYRIGHT (c) 2009 The Thomson Corporation on
STN DUPLICATE 15
AN 1994:364562 BIOSIS
DN PREV199497377562
TI Correlation between some lipophilicity characteristics of
morpholinoethylesters of 2-, 3- and 4-alkoxysubstituted phenylcarbamic

acids, and their inhibitory activity in photosynthesizing organisms.
AU Kral'ova, K.; Loos, D.; Cizmarik, J.
CS Inst. Chem., Fac. Nat. Sci., Comenius Univ., 842 15 Bratislava, Slovakia
SO Photosynthetica (Prague), (1994) Vol. 30, No. 1, pp. 155-159.
CODEN: PHSYB5. ISSN: 0300-3604.
DT Article
LA English
ED Entered STN: 23 Aug 1994
Last Updated on STN: 23 Aug 1994
AB Morpholinoethylesters of 2-, 3- and 4-alkoxysubstituted phenylcarbamic
acids (MAPC) inhibit photosynthetic processes in algae and plant chloroplasts. The inhibitory activity of MAPC in photosynthesizing organisms was in good correlations with lipophilicity
characteristics such as hydrophobic fragment constants, partition coefficients and chromatographic retention factors.

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CA SUBSCRIBER PRICE	-4.10	

-15.58

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                   Classification Data
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                   equivalents from China
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                   enhanced
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